20th Annual Meeting, American College of Chest Physicians
San Francisco, California, June 17 - 20, 1954

VOLUME XXV NUMBER 2

DISEASES

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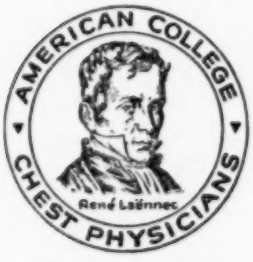

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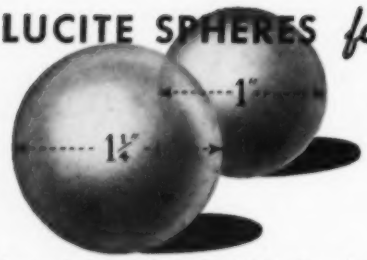

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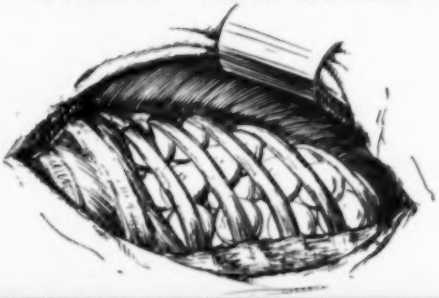

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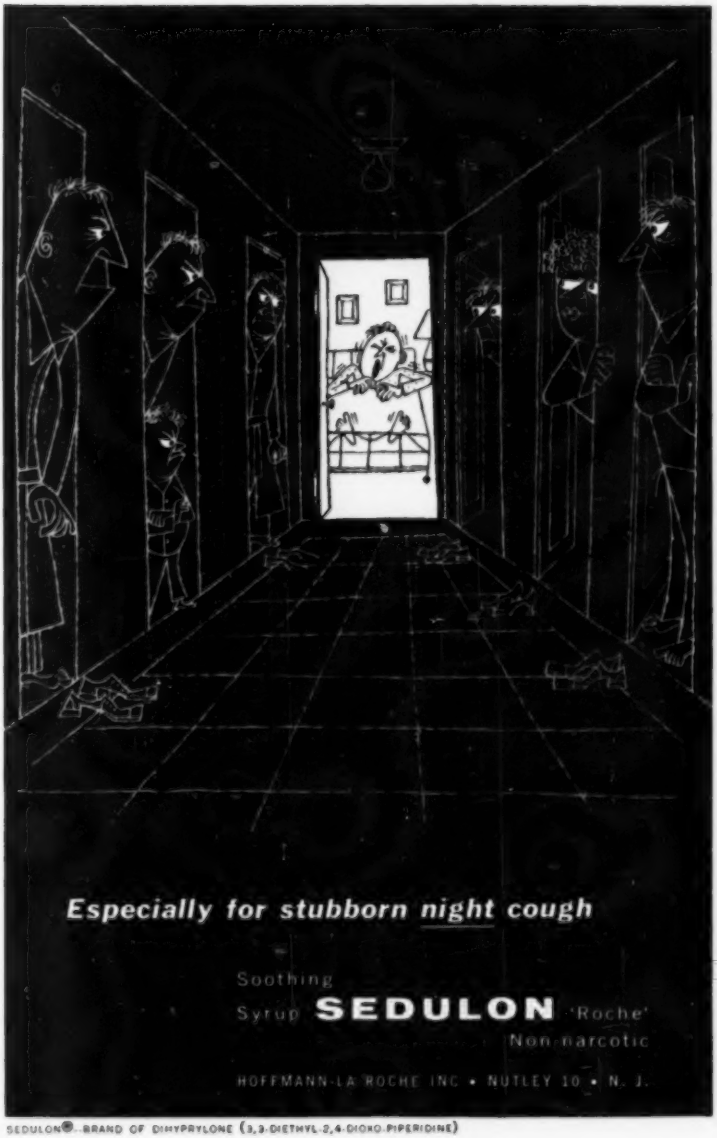

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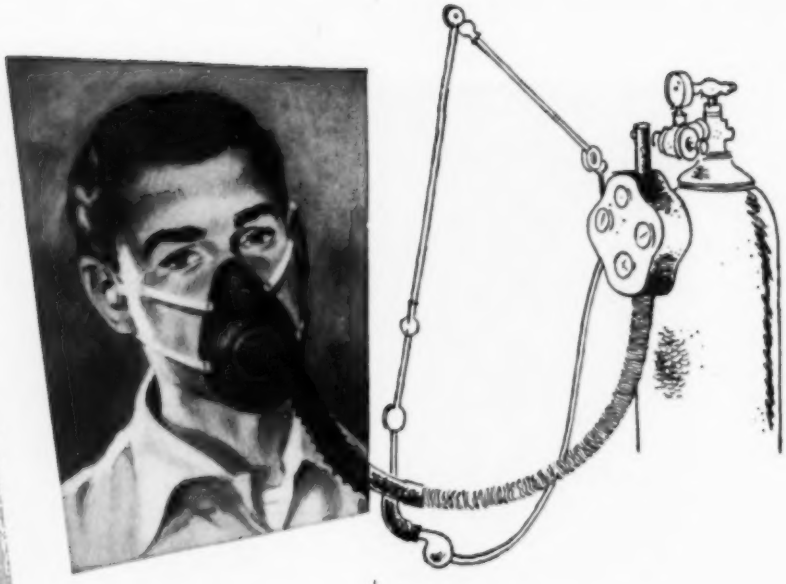

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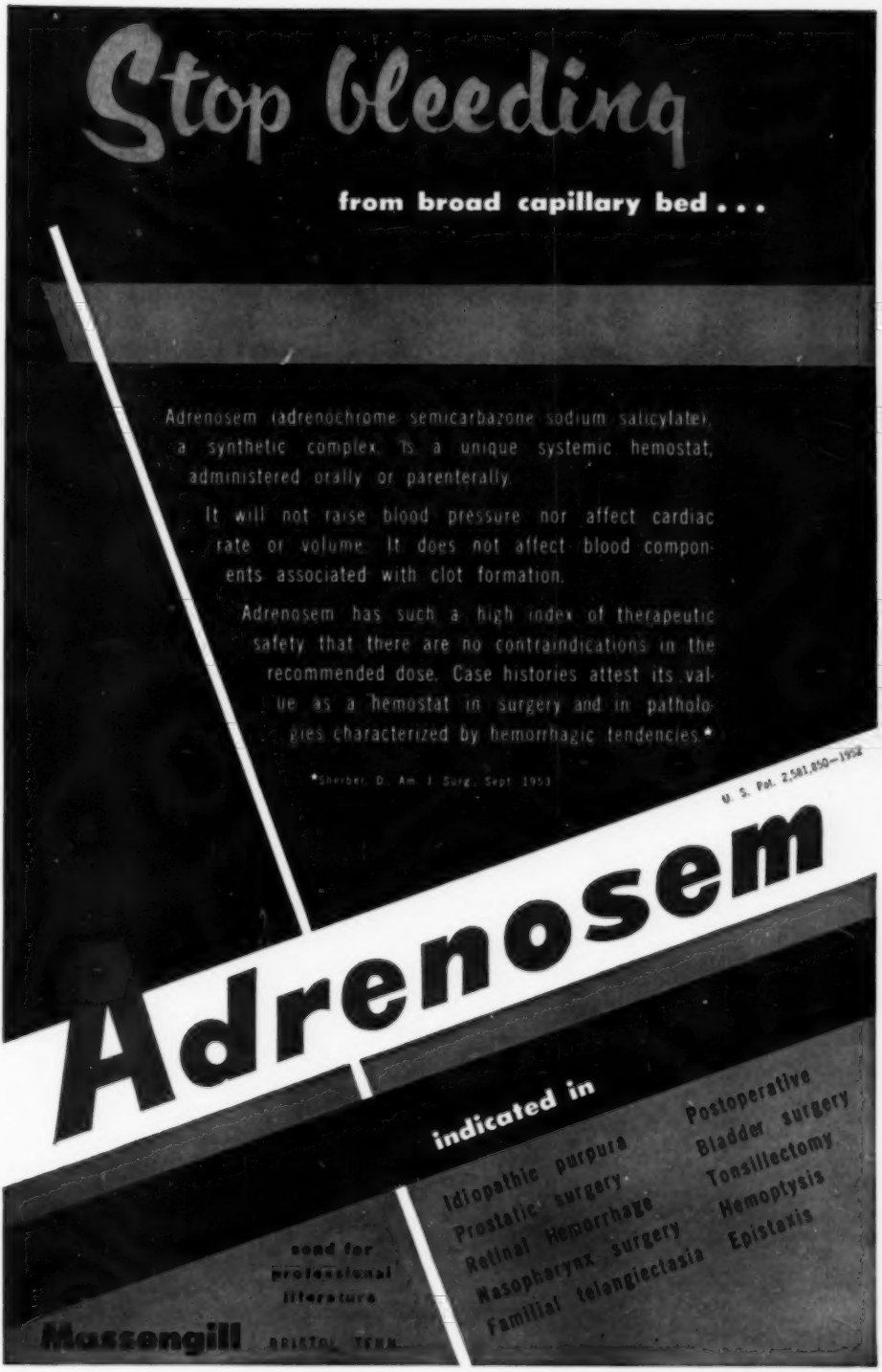
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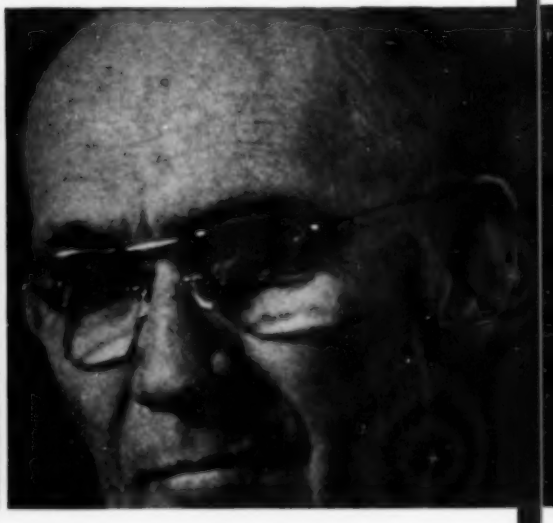

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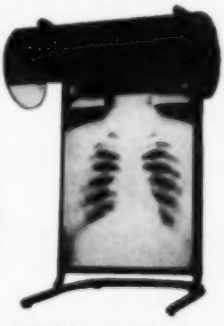

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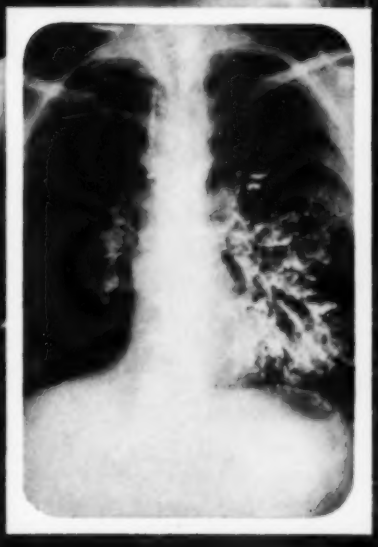

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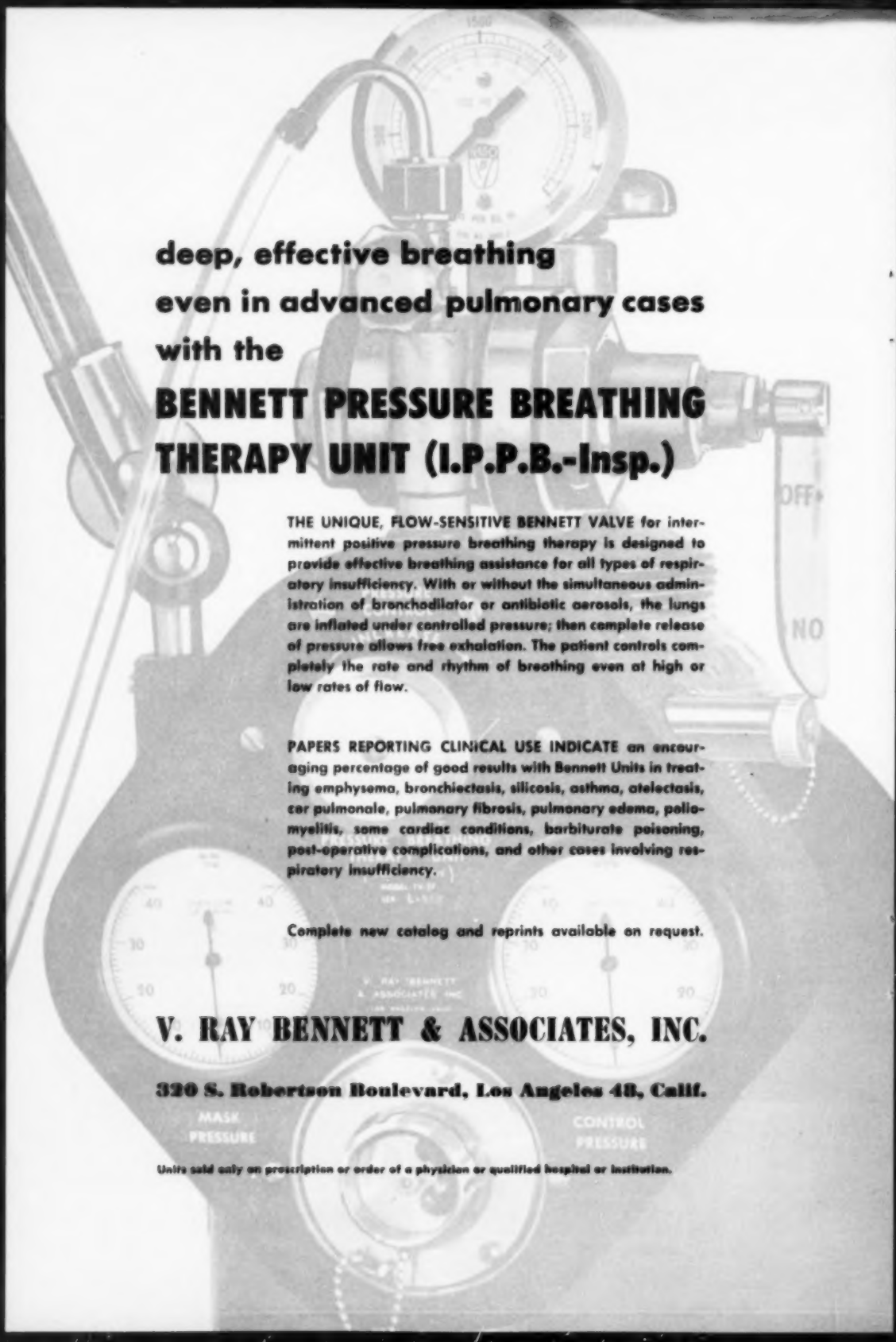

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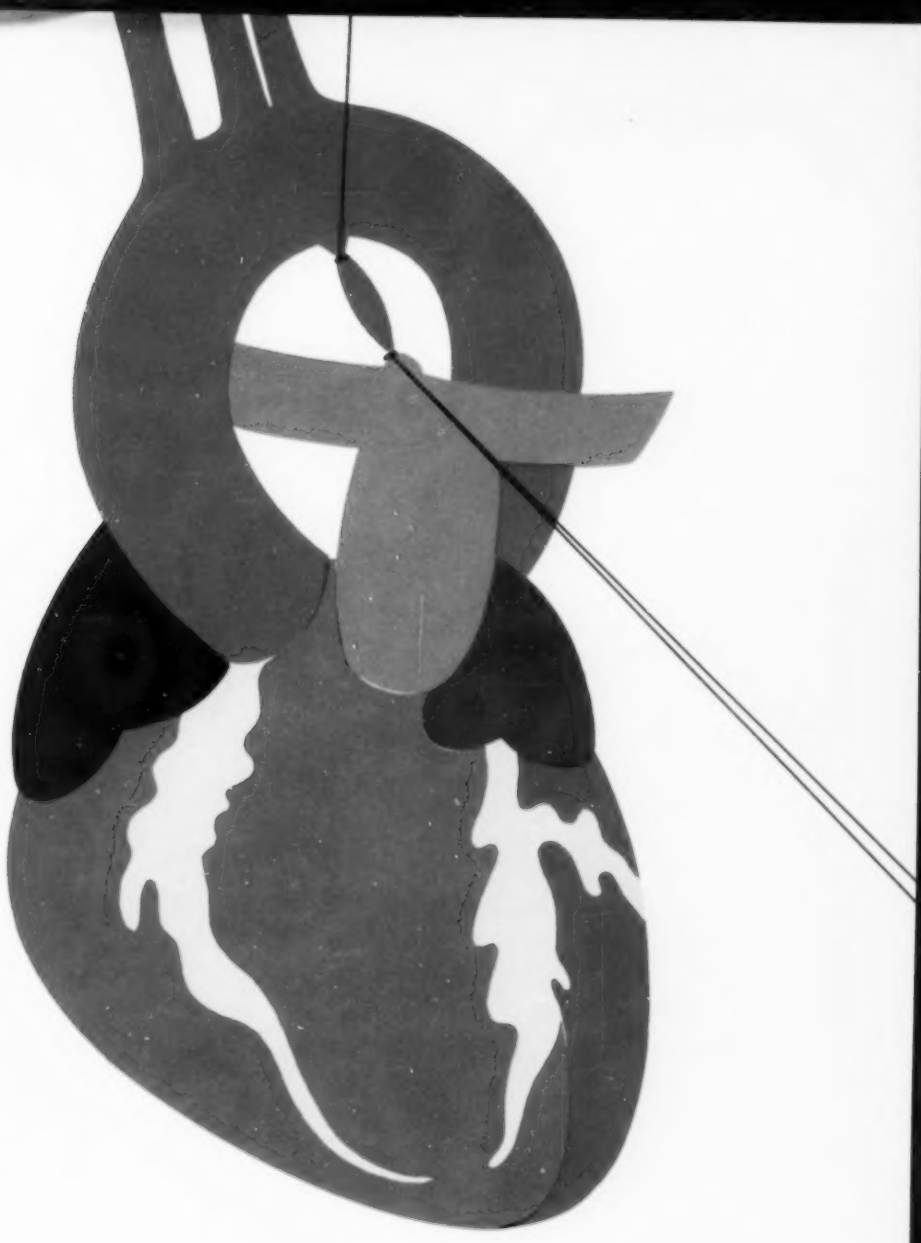

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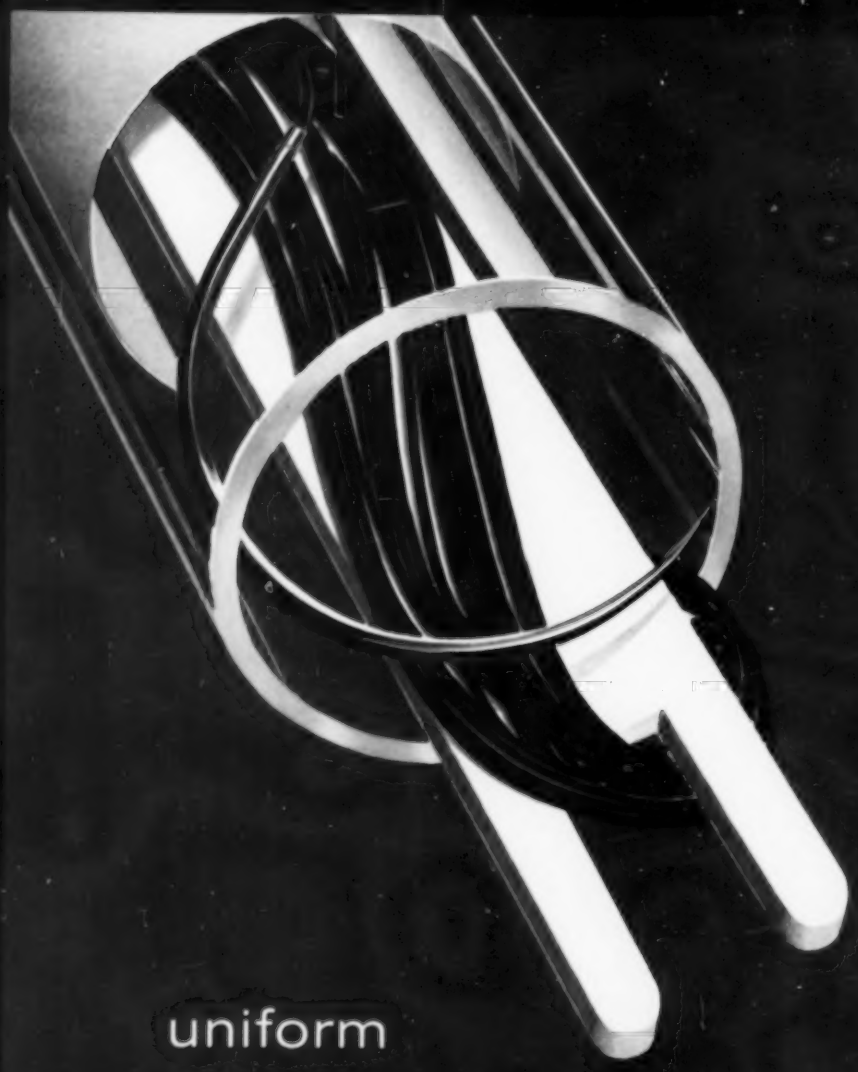

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1. Miller, J. B., and Boyer, F. H.: Jour. Pediat., 40:767, June, 1952.
2. Ravenel, S. P.: J.A.M.A., 151:707, Feb. 28, 1953.
3. Sedore, M. S.: Meeting of the Champaign County Medical Society, Champaign, Ill., March 12, 1953.

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DISEASES *of the* CHEST

VOLUME XXV FEBRUARY 1954 NUMBER 2

Angiopneumography in the Study of the Pharmacodynamic Properties of Certain Drugs

LOPO de CARVALHO, M.D., F.C.C.P.
Lisbon, Portugal

It is not enough to know the chemical constitution of a drug to be able to deduct, according to molecular groups of which it is composed, what will be the effect upon the organic functions of human beings. It is necessary to penetrate the intimate recess of its action, and, if possible, to register the disturbances it conditions at the same time, when they are produced.

From the scientific point of view it is not enough to know that some drugs produce a rise of blood pressure per arterial vasoconstriction. It is necessary to make investigations in order to reach the intimate mechanism of the process, and to be able to observe it in all its successive periods.

In some aspects of physiology and pathology, there is no difficulty to appreciate the pharmacodynamic effect of drugs. It is the case, for instance, in studying gastric digestion during normal state and pathological state. But in many other cases, the problem is not so easy to resolve, for everything happens in the intimate recess of organism, and sometimes in such a transient manner that the appreciation becomes impossible. So, investigation becomes more and more complex when the effect produced by the medicament does not show any change which could be verified by post-mortem examination.

That is what happens, for instance, with medicaments known as vasoconstrictor, or vasodilatator. How do they act upon the lesser circulation? It is difficult to give here an opinion for any used procedure to judge the phenomenon in its intimate mechanism because it may not be compatible with life and when it is, it brings such changes to the pharmacodynamic effect of the drug that an abnormal situation appears, which, of course, takes off any experimental interest.

Using the procedure which makes visible the pulmonary circulation, we can gather and register at the same time some of the main changes which many potent medicines are able to produce upon the vascular network of the lung, and upon the circulatory act itself.

I would like to present in this preliminary report, the first experiments performed at the Clinic of Pulmonary Diseases by my assistants, Carlos Vidal, Benard Guedes et Lopo de Carvalho Jr., without pretending that they should be considered, from now, as definitely setting some of the pharmacodynamic aspects we have been able to register.

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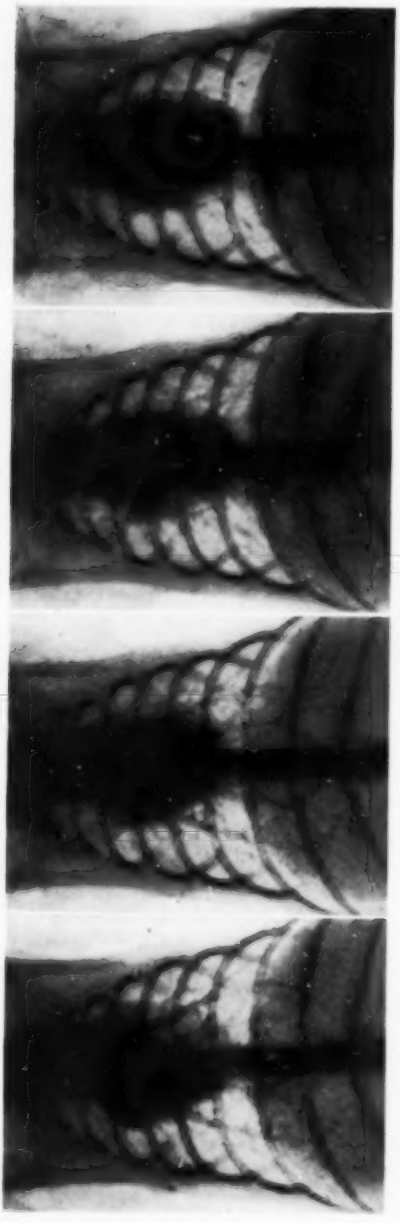

FIGURE 1

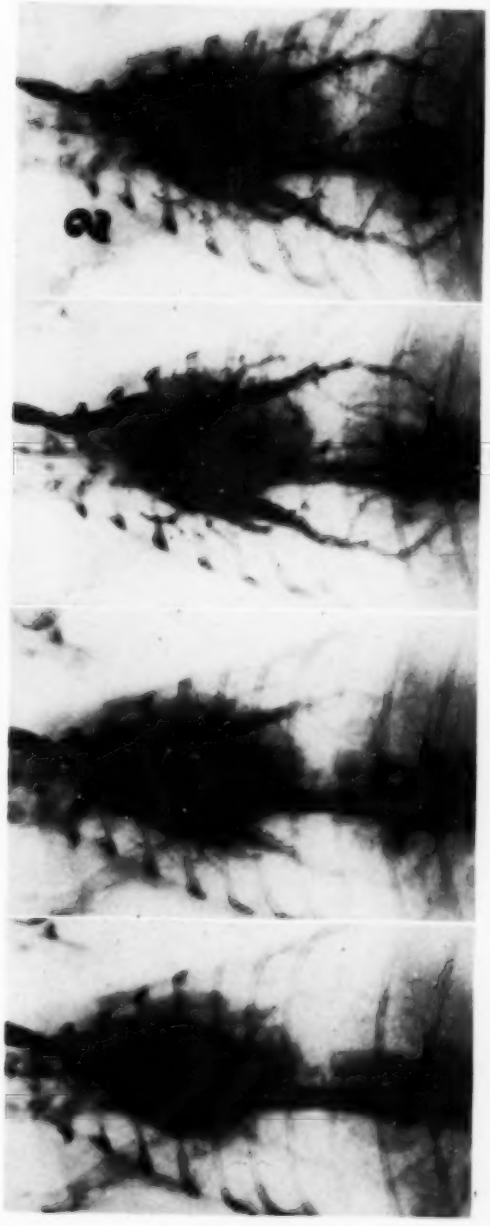

FIGURE 2

FIGURE 3

With seriographic films especially made for this experiment, we have managed to fix on the film the circulatory act in eight successive periods, at variable intervals, never less than half a second.

For these experiments, we have used the rabbit, because its pulmonary circulation is extremely fast. This is the reason why it is not suitable for every study. Nevertheless, it allows us to appreciate some of the many characteristics that some drugs exert upon the pulmonary circulation.

Here we report three experiences: the first concerning the immediate effect of adrenalin upon the pulmonary circulation, the second, pitruitrin effect and the third isonicotinic acid effect.

Sets of x-ray films reproduced as shown, help us in making a full detailed description of what we can observe.

Figure 1 is a serial angiography. The films have been taken from second to second, after an injection of 3 cc. thorotrast. It is easy to note after two seconds, that the aorta becomes visible again, what confirms the extreme velocity of the rabbit's pulmonary circulation.

We have taken from the same animal a new series of angiographs, a minute after an intravenous injection of 0.5 cc. of a millesimal solution of adrenalin. After four views, registered from second to second (Figure 2),

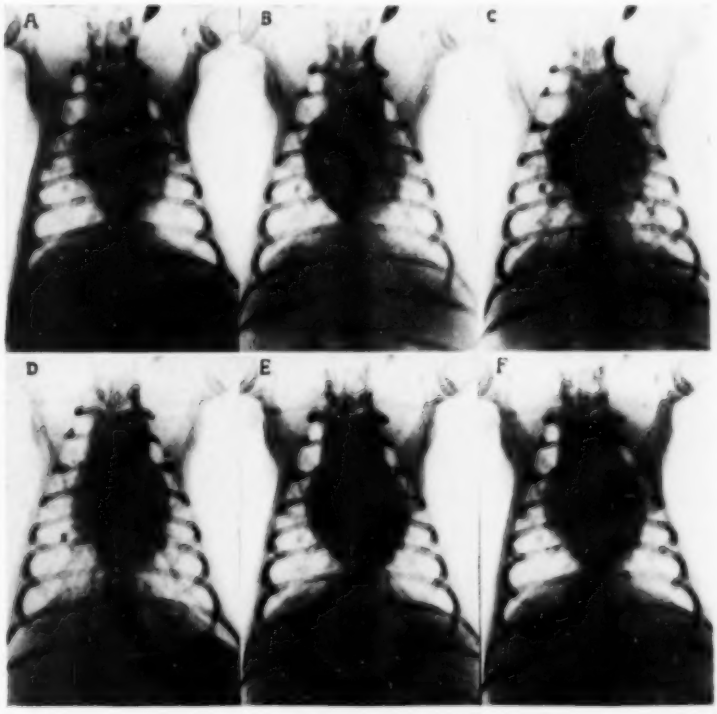

FIGURE 4

we can only perceive the arterial pulmonary circulation. Neither aorta nor venous network could appear.

Figure 3 concerns a similar experience, where pituitrin was used instead of adrenalin. The vasoconstrictor effect of this other substance is still more remarkable, and it lasts longer, for the four views were taken at five second intervals.

Figure 4 shows nicotinic acid effect. A series of six x-ray films, taken from two seconds to two seconds, after intravenous injection of 0.1 gr. of the drug, shows that this substance has a remarkable retarding action upon pulmonary circulation, for it is only after eight seconds that the aorta becomes visible again.

The determination of pulmonary circulation time after injections of these

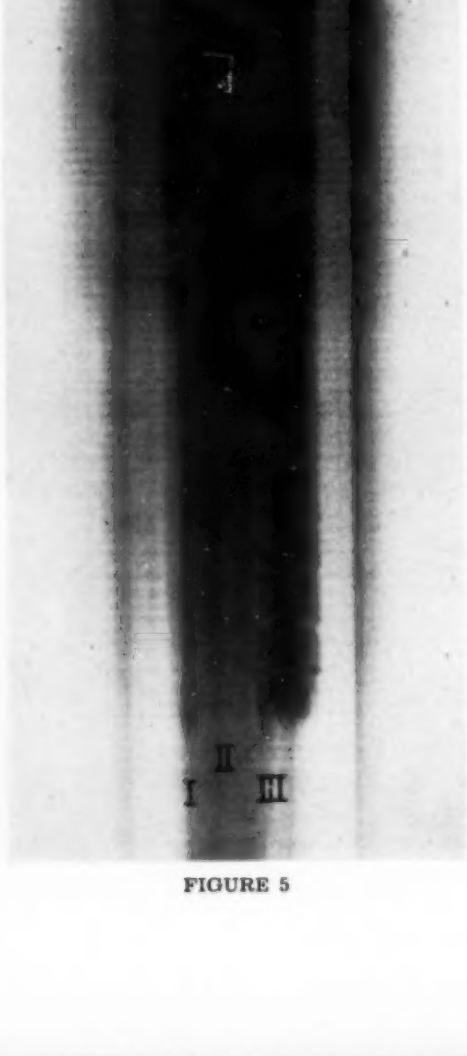

FIGURE 5

drugs confirms, as expected, the data obtained from serial angiopneumographies. For this determination, we had recourse to kymograph with simple split, already reported in "Diseases of the Chest,"* and x-ray films obtained with such a method are remarkably clear. Only the shadows of the jugular vein, right heart, and pulmonary arteries can be observed. The shadow of the aorta is not visible and the capillary circulation is hardly recognized. We have the feeling that contrast substance remained entirely in the right heart, so slow is the circulatory stream.

Take for instance, the x-ray film reproduced in Figure 5, obtained from a rabbit, after adrenalin injection in the jugular vein. The shadow of vena cava, pulmonary arteries, and right heart persists during a long trail.

These samples open large horizons and show that angiopneumography offers great possibilities to pharmacodynamic studies, especially concerning the pulmonary circulation, where so many doubts and uncertainties prevail.

SUMMARY

Here are reported the first tests carried out at the department of Pulmonary Diseases of the Santa Marta Hospital, so that the effect of certain drugs on the pulmonary circulation may be appreciated. Using the technique of angiocardiopneumography, it is possible to record in successive images some of the principal alterations that the drugs may produce in the vascular network of the lung. From the results reported, it is possible to foresee the great possibilities thus opened to pharmacodynamic studies, namely in the field of pulmonary circulation, so full of doubts and uncertainty.

RESUMEN

El autor reporta los experimentos llevados a cabo en el departamento de Enfermedades Pulmonares del Hospital de Santa Marta, con objeto de apreciar el efecto de ciertas drogas sobre la circulación pulmonar. Usando la técnica de la angicardioneumografia el autor demuestra que es posible el obtener, con imágenes sucesivas, algunas de las principales alteraciones que las drogas puedan producir en la red vascular del pulmon. Por los resultados reportados por el, es posible el prever las grandes possibilidades abiertas a los estudios farmacodinámicos, principalmente en el campo de la circulación pulmonar, tan lleno de dudas e incertidumbres.

RESUME

L'auteur rapporte les premiers essais réalisés dans le Département des Maladies Pulmonaires de l'Hôpital Santa Marta, afin d'apprécier l'effet de divers médicaments sur la circulation pulmonaire. Se servant de la technique d'angiocardiopneumographie, il demonstre la possibilité d'enregistrer à l'aide d'images successives, les modifications que les médicaments peuvent produire dans le système vasculaire du poumon.

D'après les résultats obtémis il est donc possible d'entrevoir les grandes possibilités offertes aux études pharmacodynamiques, notamment dans le domaine de la circulation pulmonaire si remplie de doutes et d'incertituds.

*Lopo de Carvalho: "Angiocardiopneumography," V.XVII, No. 3, 1950.

Loeffler's Syndrome, With a Report of Twenty Three Cases*

LOUIS MARK, M.D., F.C.C.P.
Columbus, Ohio

In 1932, Loeffler[1] described a syndrome, characterized by asymptomatic transitory pulmonary infiltration, benign course and eosinophilia. Much has been written regarding this syndrome in recent years. Many of the reported cases, however, present definite symptoms and the question has frequently arisen as to whether these cases are similar to those Loeffler described. This disease has taken on much greater importance because of the difficulty in differentiating it from other pulmonary diseases, especially tuberculosis and malignancy.

The cause of the condition has not been clearly defined. Some describe it as a syndrome produced by a tuberculous process while others ascribe an allergic etiology with asthma and other hypersensitivites frequently present. Helminthiasis has also been suggested as a cause, but in recent years many cases of Loeffler's Syndrome have been diagnosed where parasites have not been found.

The similarity to Tropical eosinophilia has been noted. The blood pictures are similar but pulmonary findings are usually absent in this disease although occasionally there may be some mottling in both lung fields on x-ray films

In the 23 cases herein reported, few were asymptomatic. Many had asthmatic syndromes or bronchospasms; cough was frequent; loss of weight and expectoration occurred in some, but this was not particularly characteristic and over half carried fever. No fatality occurred and in the majority of the cases, the lesion cleared rather rapidly. Until recent years no treatment for the condition has been known and most of the cases cleared spontaneously, occasionally recurring.

Review of the Literature

Binda and Weinberg[2] reported two cases in 1940, and concluded that the infiltration and eosinophilia were of tuberculous origin. They suggested prolonged observation. Cattaneo[3] reported one case in 1940 and concluded that "the etiopathogenesis of this disease is not known. Some have attributed it to intestinal helminthiasis but this is not easy to prove." Bauman[4] reported a case with pleural effusion. Cruciani and Noguera[5] said, "According to Hajos, the Eosinophilia resulting from increased allergy leads to Vagotonia, bronchospasm and concomitant atelectasis, according to Engel, hypersensitivity causes alveolar and bronchial edema and finally complete obstruction of the bronchial lumen with resulting atelectasis." They con-

*Presented at the II International Congress on Diseases of the Chest, American College of Chest Physicians, Rio de Janeiro, Brazil, August 30, 1952.

clude by saying, "Loeffler's Syndrome is to be considered as a tissular and humoral reaction on the basis of hypersensitivity, of tuberculous or other origin; it may correspond to primary or tertiary tuberculosis or to allergic manifestations of various kinds." Glenn[6] presented three cases of infiltrations of transient nature easily mistaken for pulmonary tuberculosis. He concluded, "It is suggested that diseases of this type be called sub-acute pneumonitis until a more correct name can be given."

Apley and Grant[7] report eosinophilia with pulmonary disease on return from the tropics and give the differentiation between Loeffler's Syndrome and tropical eosinophilia. They state "The contrast between the climates in which the two conditions are described is striking. Nevertheless, a typical example of tropical eosinophilia, occurring in the dry climate of Egypt, has recently been recorded, and conversly a case of Loeffler's Syndrome occurring outside of Europe had a previous history of bronchitis related to humidity."

Wright, Gold and Jennings[8] presented the incidence of pulmonary consolidations in the mild asthmatic. They stated "These 24 cases are difficult to classify, because they do not conform strictly to the allergic consolidations described by Loeffler or to virus (atypical) pneumonia . . . In all instances the roentgen shadows were indistinguishable from the infiltration seen in mild virus pneumonia and most frequently appeared in the lower lung fields."

Pujo[9] said "Certain roentgenographical findings in whooping cough have been considered as belonging to this syndrome." Herbert, DeVries and Rose[10] found a rapid drop in the eosinophile count after the administration of ACTH and also noted changes on serial x-ray films. Reeder and Goodrich[11] in reporting four cases stated "The protean manifestations of the condition and its association with other pathologic states, necessitates a broadening of our concepts. Pulmonary infiltration with eosinophilia is attributable to many agents . . . Loeffler's Syndrome is at present used to indicate evanescent pulmonary infiltrates in persons with little or no illness. A descriptive classification which is more inclusive may prove useful in conditions of similar origin having greater duration and dangers."

Buckles and Lawless[12] reported a case of pneumonectomy in which the diagnosis prior to surgery was carcinoma. They also noted a satisfactory response to surgical extirpation of a persistent eosinophilic granuloma of 14 months' duration.

From these reviews of the literature, it can be seen that many cases reported as Loeffler's Syndrome do not actually fit the description originally set out by Loeffler. Many of them have symptoms, fever and no helminthiasis. One can only conclude that a more inclusive classification of a transitory pulmonic lesion with eosinophilia must be found. If the cases herein reported are to be included, they must be considered as Loeffler's Syndrome or as an entirely separate disease entity.

Loeffler described his cases as asymptomatic. Many patients complain of cough, asthmatic syndromes, expectoration, loss of weight, fatigue, fever, and shortness of breath. Pain over the sternum is a fairly frequent

CHART I

Case No., Age, Sex	Tuber-culin	Major Symptoms	Allergies	Blood Eosinophiles	Stools	Sputum
1, N.S., 60, F.	pos.	Cough, expectoration, fever, loss of weight, short of breath.	Negative	14 (21%)	Negative	Neg.
2, D.K., 51, M.	pos.	Short of breath, cough and wheeze.	Negative	(16%)	Negative	Neg.
3, C.L., 49, M.	pos.	Wheezing and cough.	Mild, unimportant reactions	12 (64%)	Negative	Neg.
4, R.K., 26, F.	pos.	Tired, loss of weight and cough.	Not done	(13%)	Not done	Neg.
5, S.L., 64, F.	pos.	Weakness, cough, weight loss and wheezing.	Not done	(12%)	Not done	Neg.
6, C.B., 52, F.	pos.	Cough, expectoration and wheezing.	Few mild positives	2 (21%)	Negative	Neg.
7, J.B., 39, M.	pos.	Cough, expectoration, loss of weight and fever.	Not done	(26%)	Negative	Neg.
8, O.B., 46, F.	pos.	Cough, expectoration, wheezing, fever, weight loss.	Not done	8 (29%)	Negative	Neg.
9, S.M., 13, F.	neg.	Fever, tired, severe cough, wheezing.	Negative	(11%)	Negative	Neg.
10, E.F., 41, F.	pos.	Asthma, cough, short of breath.	Many positives	(14%)	Negative	Neg.
11, J.A., 46, M.	pos.	Cough, pain in chest and tired.	Negative	(16%)	Negative	Neg.
12, C.J., 20, F.	neg.,	Diabetes, cough and fever.	Negative	(19%)	Ascaris	None
13, M.S., 29, F.	pos.	Recurring bronchospasms.	Negative	(13%)	Negative	None
14, W.P., 9, M.	neg.	Fever, chills, tired and cough.	Negative	(11%)	Ascaris	None
15, L.W., 63, M.	pos.	Cough, short of breath and tired.	Not done	(14%)	Negative	Neg.
16, H.G., 42, M.	neg.	Bronchospasms, weight loss and pains in chest.	Not done	(14%)	Not done	Neg.

CHART I (Continued)

Case No.	Fever	X-ray	Treatment	Results	Comments
1	101.0	Shifting shadow right second and left apex.	Blood transfusions.	Cleared, no recurrences.	Patient responded rapidly with clearing of shadows, drop in temperature and clearing of symptoms.
2	98.4	Patchy densities.	Adrenalin, blood transfusions.	Cleared slowly.	Recurrences up to four years ago. None since.
3	104.8	Massive pneumonitis.	Blood transfusions.	No recurrence. Cleared.	Patient critically ill, no response to antihistomine or antibiotics. Responded rapidly to blood transfusions.
4	99.2	Localized density.	None	Cleared.	No recurrence.
5	99.6	Extensive densities.	Adrenalin.	Cleared.	Treated four months, cleared, no recurrence.
6	99.8	Recurring patchy shadows.	Adrenalin, blood transfusions. Cortisone.	Cleared, frequent recurrence.	This patient had several recurrences in eight years. None since use of Cortisone.
7	100.5	Recurring massive densities.	Treated for Tuberculosis two years.	Cleared.	Sanatorium care 3 times, total 2 transfusions. On 4th recurrence diagnosed Loeffler's not tuberculosis.
8	103.8	Massive shifting shadow.	Adrenalin.	Cleared.	No recurrences.
9	102.0	Patchy shadows.	Cortisone.	Cleared.	Symptoms and fever of 4 mos. duration. No response to treatment but cleared rapidly with Cortisone.
10	98.6	Recurring patchy shadows.	Cortisone.	Cleared.	Patchy areas cleared rapidly. No recurrence after one year.
11	98.6	Recurring densities.	Blood transfusions. Cortisone.	Still has recurrence every 6 to 10 months.	Patient still has reoccurrences every 6 to 10 mos.
12	101.0	Recurring shadows.	Blood transfusions.	Still has recurrences.	Could not tolerate Cortisone or A.C.T.H. Clears with blood transfusions but has recurrences.
13	102.0	Patchy shadows.	Cortisone.	Cleared.	No recurrences in 2 years.
14	103.0	Patchy shadows.	Cortisone.	Cleared.	No recurrences.
15	98.4	Patchy shadows.	Cortisone.	Cleared.	Have not seen patient since treatment.
16	98.6	Patchy shadows.	Cortisone.	Cleared.	Had one recurrence.

complaint. Cough is mostly of the explosive or asthmatic type. In the majority, expectoration is very scanty but in some it is profuse, lasting for several weeks and disappearing when the cough clears. If we are to include all shifting shadows with eosinophilia as cases of Loeffler's Syndrome, we must adopt the concept that some are symptomatic and follow a definite pattern.

In a large percentage of cases, physical examination is not of any great value. Frequently wheezing is noted but breath sounds, as a rule, are fairly normal. In cases with sputum, rales are often found localized posteriorly in the bases of the lungs.

In the literature, references are constantly made to allergies. The majority of these patients report that allergy tests had been performed previously with very few positive reactions to allergens. In those cases with allergies actually found, elimination of the offending substances failed to clear up the symptoms. Undoubtedly allergies play a part but we feel that their role is minor in the development of the pulmonary changes.

In the original reports, helminthiasis was found in all cases. Possibly in the cases originally described by Loeffler, this etiology played an important part. In our series of cases, only 13 per cent revealed parasites.

The blood picture is of utmost importance. The percentage of eosinophiles varied from 8 to 64 per cent. Eosinophilia, however, is not directly related to the severity of the symptoms or to the extent of the x-ray shadows. It was noted that the highest percentage of eosinophiles seemed to occur just before the lesion started to recede rather than when the fever was the highest or when the symptoms were at their peak. As the

CHART I (Continued)

Case No., Age, Sex	Tuberculin	Major Symptoms	Allergies	Blood Eosinophiles	Stools	Sputum
17, M.R., 27, F.	pos.	Tired, cough and and poor appetite.	Not done	(21%)	Ascaris	Neg.
18, W.K., 36, M.	pos.	Cough, expectoration, tired and weight loss.	Negative	(12%)	Negative	Neg.
19, J.T., 41, M.	pos.	Short of breath, bronchospasms, and tired.	Negative	(16%)	Negative	Neg.
20, A.T., 55, M.	pos.	Wheezing, tired and cough.	Negative	(10%)	Negative	Neg.
21, G.R., 33, F.	pos.	Cough, wheezing, short of breath and tired.	Negative	13 (23%)	Negative	Neg.
22, T.I., 9, M.	neg.	Fever, cough and enlarged glands.	Negative	(8%)	Negative	None
23, R.L., 48, M.	pos.	Cough, wheezing, short of breath.	House dust	(17%)	Negative	Neg.

lesion cleared, the eosinophiles often dropped to below one-half of one per cent. Otherwise the blood count was fairly normal.

X-Ray Findings

It is difficult to describe the x-ray findings in Loeffler's Syndrome due to the great variation in different cases. A large percentage are similar to tuberculous lesions. Some shadows may appear as excavations but careful study will prove them to be simple infiltrations. In those x-ray films the lesion is either pneumonic or atelectatic. Even where the appearance is atelectatic there is little of the usual shifting of structures suggesting a constriction of that portion of the lung.

Most of our cases revealed infiltration, localized usually in the lower two thirds of the lungs. These had a cylindroid or patchy appearance suggesting a blocking of some of the smaller bronchi. Their appearance was considerably different than the infiltrations of bronchopneumonia but, somewhat similar to virus pneumonitis. When the densities occurred in the extreme lower lobe, suggestion of atelectasis was quite marked. It was also noted that when patchy appearing parenchymal shadows were present, the patient invariably had pain over the sternum with frequent broncho-spasms and dry cough. When the densities were localized in the extreme lower lobe along the main stem bronchi, expectoration was present.

Presentation of Cases

Twenty-three cases were diagnosed as Loeffler's Syndrome and treated accordingly. These cases are briefly outlined in Chart I. We wish to present in greater detail, four cases of this group because of the variance in symptoms and x-ray film appearance.

CHART I (Continued)

Case No.	Fever	X-ray	Treatment	Results	Comments
17	98.6	Patchy shadows.	Cortisone.	Cleared.	Gained weight, 24 lbs. in 2½ mos. No recurrences.
18	98.6	Areas of atelectasis.	Blood transfusions.	Cleared.	No recurrences.
19	98.6	Patchy densities.	Blood transfusions. Cortisone.	Shadows cleared.	Shortness of breath remained, spasms cleared.
20	98.6	Density suggesting atelectasis.	Cortisone.	Cleared.	No recurrences.
21	98.6	Shifting shadows.	Blood transfusions. Cortisone.	Cleared, one recurrence.	Response to Cortisone rapid and complete. No recurrences after Cortisone treatment.
22	100.0	Patchy shadows.	Cortisone.	Cleared.	Signs, symptoms and x-rays cleared in 3 days.
23	99.8	Small patchy shadows.	Cortisone.	Cleared, no recurrences.	Cleared rapidly.

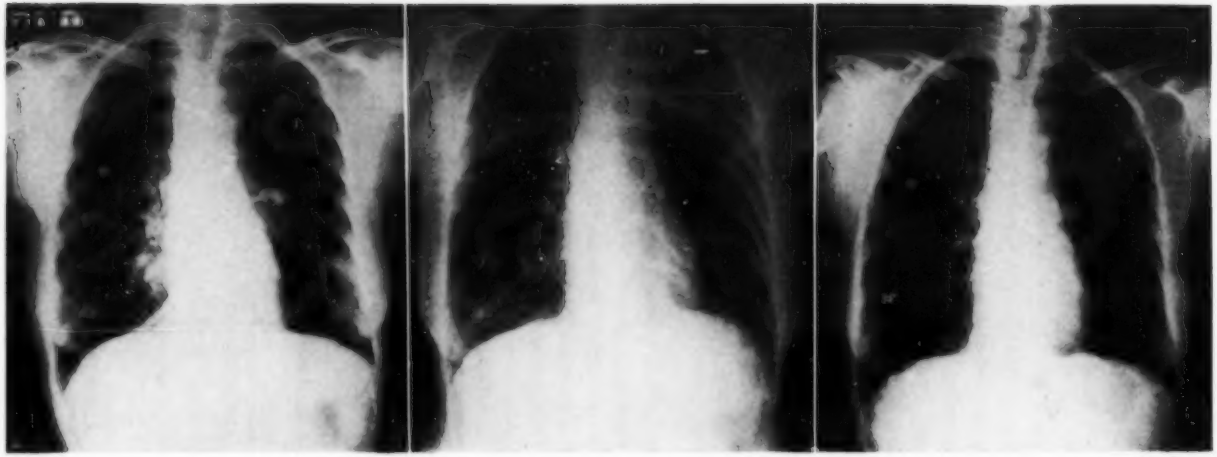

FIGURE 1A FIGURE 2A FIGURE 3A

1A, October 18, 1949: Infiltration, left apex, suggestive cavity.
2A, October 28, 1949. Flat density, left apex. Infiltration right midfield.
3A, November 28, 1949: Left clear, infiltration right second interspace.

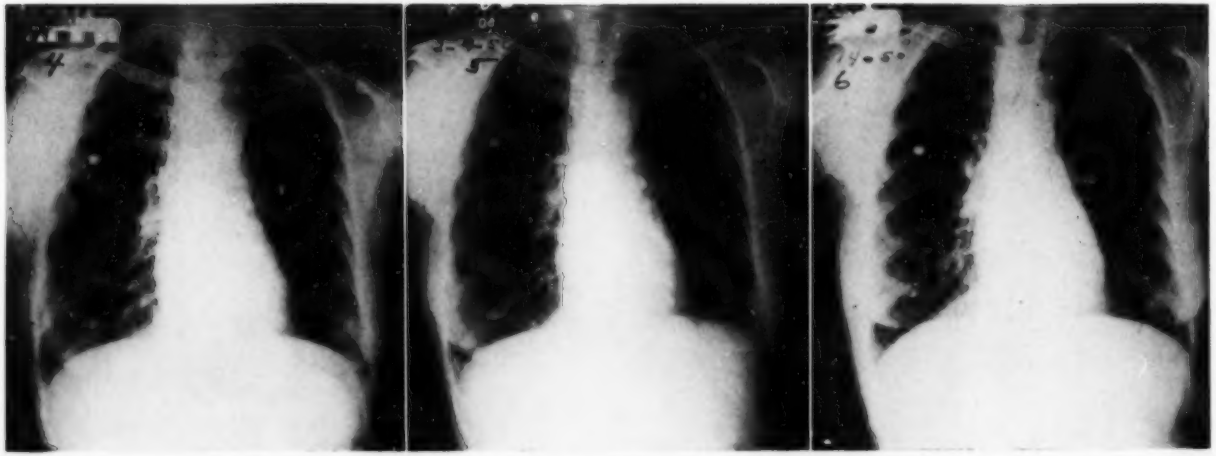

FIGURE 4A FIGURE 5A FIGURE 6A

4A, January 2, 1950: Infiltration shifted to left midfield.
5A, February 9, 1950: Infiltration left third interspace.
6A, March 14, 1950: Lungs clear.

Case 1: N.S. White female, age 60, was first seen on October 21, 1949, with a history of five attacks of pneumonia in 11 years. Each attack lasted from two to five months. During this time she carried fever, severe cough, profuse expectoration, rapid pulse, loss of weight, shortness of breath, poor appetite and marked exhaustion. A diagnosis of tuberculosis was made in September, 1949 and prolonged bed rest advised.

On examination we found a poorly nourished white female, with congested throat, wheezing throughout both lungs, loud mucous rales at both bases posteriorly heart sounds rapid with no murmurs,, vital capacity 1,400 cc., blood pressure 116/80, temperature 101 degrees F., and sputum negative for tubercle bacilli. Allergy tests were negative, stools negative for ova and parasites, blood

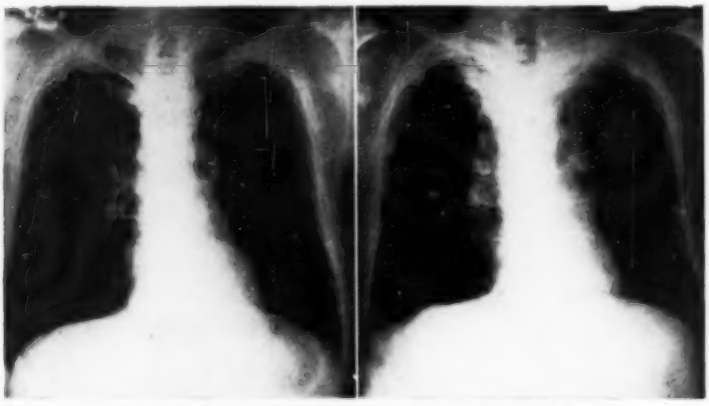

FIGURE 1B FIGURE 2B

1B, June 7, 1947: Slight cloudiness both apexes.
2B, July 10, 1947: Increase bilateral apical densities.

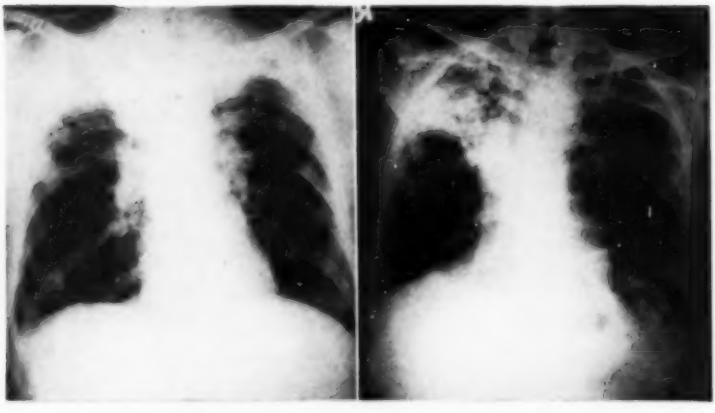

FIGURE 3B FIGURE 4B

3B, July 14, 1947: Marked extension of upper lobe densities.
4B, July 18, 1947: Further increase.

FIGURE 5B FIGURE 6B FIGURE 7B

5B, July 29, 1947: Entire left lung and upper half of right lung pneumonic appearance.

6B, July 30, 1947: Clearing after first blood transfusion.

7B, September 15, 1947: Lungs clear except for small shadow right second interspace.

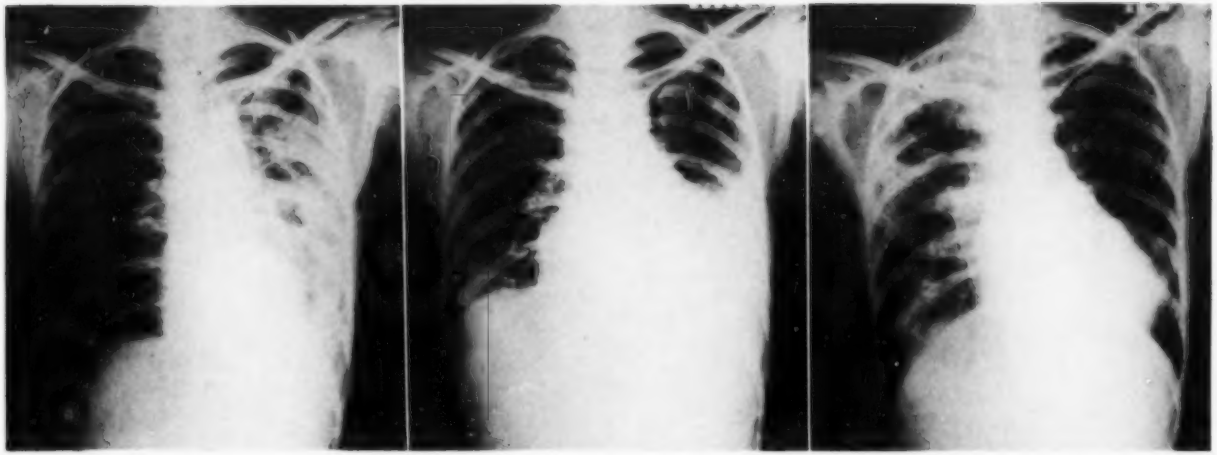

FIGURE 1C FIGURE 2C FIGURE 3C

1C, May 6, 1945: Extensive involvement left lung with suspicious cavitation.
2C, June 26, 1946: Lesion cleared, heart dilated, fluid left pleural cavity.
3C, August 5, 1946: Left lung clear, fluid gone, heart reduced in size, infiltration right lung.

count normal except for 11,000 white cells per cubic mm., with 14 per cent eosinophiles. The first x-ray film showed evidence of infiltration at the left apex suggestive of tuberculosis.

A diagnosis of Loeffler's Syndrome was made mostly on the basis of the history, eosinophile count and negative sputum.

The patient was hospitalized on October 26, when she received 500 cc. of whole blood intravenously and on October 28, 250 cc. of whole blood, which was repeated on October 30. Symptoms began to clear rapidly after the first blood transfusion and disappeared completely by October 30. On November 3, 1949, an x-ray film of her chest revealed that the lesion in the left apex had cleared.

Even though she remained symptom free, the fact that she had had so many recurrences, a protective blood transfusion of 500 cc. of whole blood was given on January 20, 1950 and 250 cc. three days later. This was repeated in March, 1950. She gained approximately 30 pounds, lost her cough, expectoration and wheezing and felt perfectly well. She has had no recurrence of symptoms and her x-ray films have been clear.

Case 3: C.L., was first seen on July 16, 1945. He had been having intermittent attacks of asthma and bronchospasms with shortness of breath on exertion. A diagnosis of asthma was made. Allergy tests were performed which were negative. Chest x-ray films were essentially clear. The blood count revealed 4 per cent eosinophiles. A diagnosis of early emphysema with bronchospasm was made.

In June 1947, he had a severe attack which was again diagnosed as asthma and he was rushed to a hospital for treatment. Allergy tests were repeated and again proved negative.

X-ray film of the chest was essentially clear. During treatment, cough and expectoration persisted and further x-ray studies revealed changes in the apices which were suggestive of early tuberculosis. Fever, cough and expectoration became more severe and he received antibiotic therapy. He did not appear to be tuberculous and a suspicion of early carcinoma was entertained. Bronchoscopy was essentially negative. Sputum remained negative for tubercle bacilli. Blood count showed 50 per cent eosinophiles. Stools were negative. The skin was exceptionally dry and lesions were present in the mouth. He had a septic type of temperature ranging from 98 in the morning to 104 degrees F. in the afternoon. He

FIGURE 4C FIGURE 5C

4C, August 25, 1946: Increased involvement right lung. Infiltration left lung.
5C, September 26, 1946: Right lung clearing, entire left lung involved.

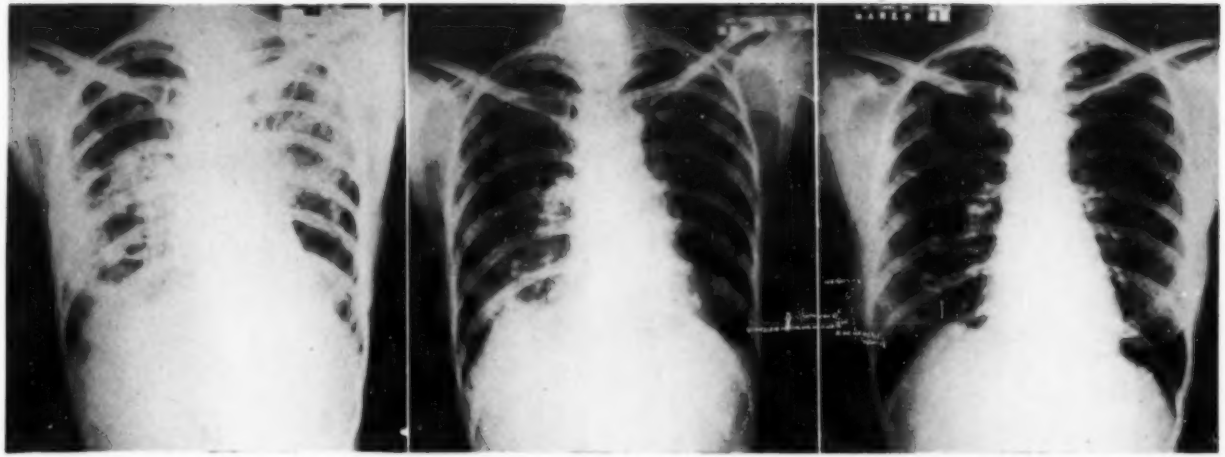

FIGURE 6C FIGURE 7C FIGURE 8C

6C, October 21, 1946: Left lung clearing, both lungs involved.
7C, November 30, 1946: Lungs clearing, heart reduced in size.
8C, March 27, 1947: Lungs clear, heart size normal.

responded poorly to antibiotics and to antihistaminics. The eosinophile count went up to 64 per cent. The prognosis appeared to be poor.

A diagnosis of Loeffler's Syndrome was made. He continued to grow weaker.

At this point a blood transfusion of 500 cc. of whole blood was given and he immediately improved. Another 500 cc. was given on the following day and x-ray film showed rapid clearing of the lesion. The eosinophile count dropped from 64 to 1 per cent within 48 hours. Blood transfusion was again repeated the third day. The x-ray findings cleared in eight days and the clinical picture continued to improve rapidly. The temperature returned to normal and he was discharged from the hospital nine days after the first blood transfusion was given.

A blood transfusion was given six weeks later even though the lung fields were clear and he was symptom free. This patient was seen in October, November and December of 1947 and the lungs remained clear with no recurrence of the asthmatic syndrome.

The x-ray films showed that the lesion started in both apices and seemed to have uniform bilateral spread downward, eventually filling almost the entire left lung and the upper half of the right lung.

He remained well for a considerable period of time but died after a kidney ailment. No necropsy was performed.

Case 8: O.B., was admitted to the Rocky Glen Sanatorium for tuberculosis in 1946 with the history of cough, expectoration, loss of weight, fever, shortness of breath and marked wheezing. Symptoms had been present for about five months. Sputums had been negative but x-ray films revealed what appeared to be an extensive lesion throughout the entire left lung with multiple cavitation.

On admission to the sanatorium, coughing was severe and expectoration was profuse, temperature spiked to 103 degrees F. in the afternoons. Sputum and gastric washings were negative for tubercle bacilli. Allergy tests were negative, white count was 15,000 with 8 per cent eosinophiles.

The patient had all the characteristic symptoms of tuberculosis except for positive sputum. The 8 per cent eosinophiles at the time of admission was considered higher than normal but not particularly significant.

We suspected atelectasis of the left lung and a bronchogram was attempted. During the instillation of the local anaesthetic in the throat, she developed a coughing spasm, became very short of breath with an acute dilatation of the heart. Her condition was quite critical. Oxygen and adrenalin were administered. She recovered rather slowly. An x-ray film taken 48 hours later surprisingly revealed the entire left lung to be clear, the heart extremely dilated and some pleural effusion at the left base. The eosinophile count at this point was 21 per cent. Two days later it was 29 per cent. A diagnosis of Loeffler's Syndrome was made and in the absence of any known treatment, she was given four minims of 1:1000 adrenalin by injection every four hours for about three months.

A series of x-ray films (Figures 1B to 8B) gives evidence of the rapid shifting of the shadows. The lesion started on the left side, shifted to the right, then both lungs were involved, with eventual resolution. The entire course ran approximately four months and when the eosinophile count began to drop, shadows in the lungs began to clear, the wheezing stopped, she gained 40 pounds, and the shortness of breath began to subside.

The patient has had no recurrence. The heart function has returned to normal. Subsequent x-ray films appear clear and the eosinophile count has not been above 6 per cent.

This case is different from the others in that new shadows occurred before the old lesion had completely cleared. There was also recurrence of the original densityes. All portions of both lungs were involved at some time during the course of the illness.

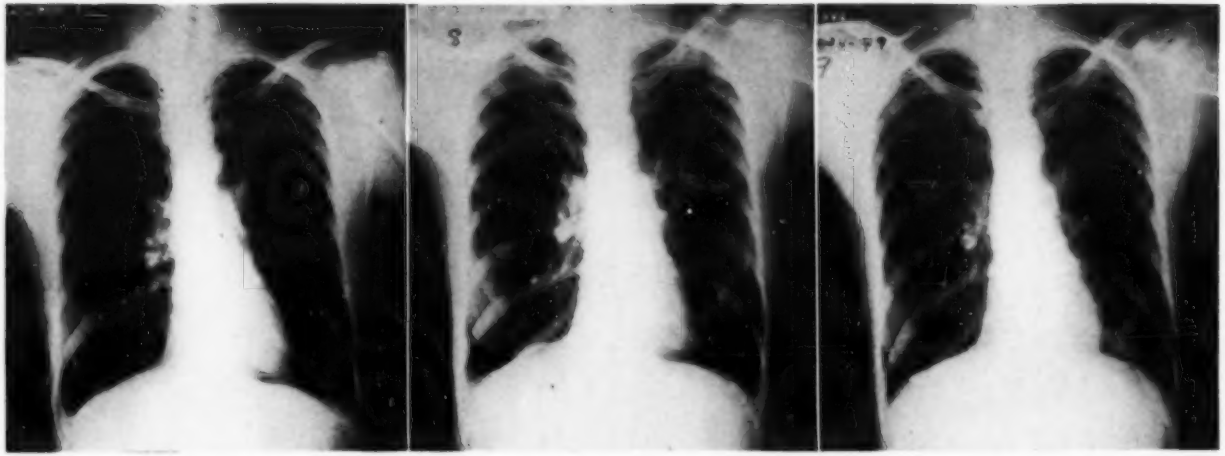

FIGURE 1D FIGURE 2D FIGURE 3D

1D, November 22, 1948: Lungs clear.
2D, June 14, 1949: Infiltration, left third interspace.
3D, June 24, 1949: Left clear, infiltration right midfield.

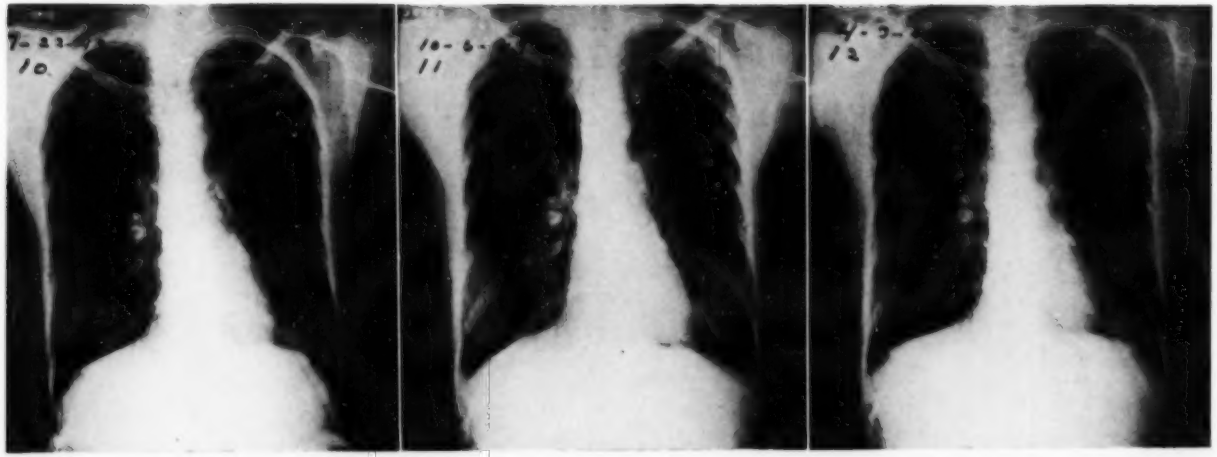

FIGURE 4D FIGURE 5D FIGURE 6D

4D, July 22, 1949: Lungs clear.
5D, October 6, 1949: Recurrence left second interspace.
6D, April 3, 1950: Lungs clear.

Case 21: Mrs. G.R., 38 years old, seen on June 24, 1949, gave a history of being treated for tuberculosis. The diagnosis was based upon prolonged exposure to her husband, who had had thoracoplasty for active tuberculosis. She stated that she had recurrent asthma all her life. Often a lesion would clear only to be replaced by a new one in a new portion of the chest as shown on x-ray films.

When first seen by us on June 24, 1949, she gave a history of wheezing, some loss of weight, shortness of breath and scant expectoration.

Examination revealed that she was poorly nourished. Harsh wheezing was heard throughout both lungs and rales were present at both bases posteriorly. The heart rate was rapid with no murmurs. Tuberculin test was positive and her sputum was negative for tubercle bacilli. Vital capacity was only 1100 cc.

X-ray films revealed evidence of localized infiltration in the midportion of the right lung. Comparing this film with those taken prior to her coming to us re-

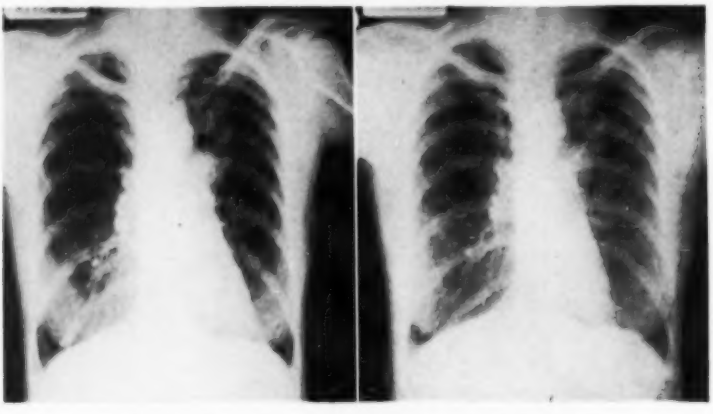

FIGURE 7D FIGURE 8D

7D, November 20, 1950: Infiltration left upper and near right hilus.
8D, November 21, 1950: Twelve hours after Cortisone treatment, no change.

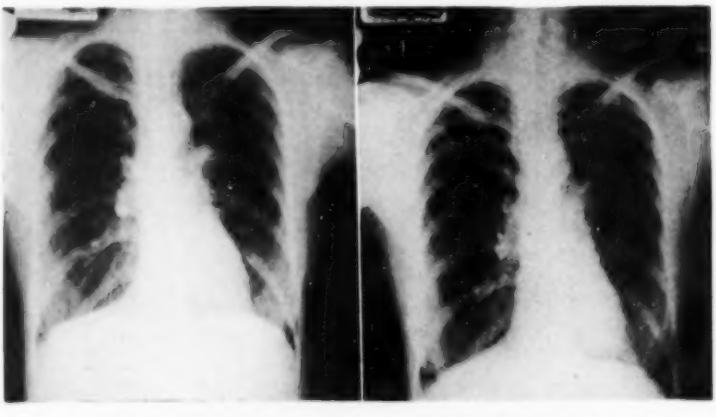

FIGURE 9D FIGURE 10D

9D, November 22, 1950: Thirty-six hours after Cortisone treatment started.
10D, November 23, 1950: Forty-eight hours after Cortisone treatment started

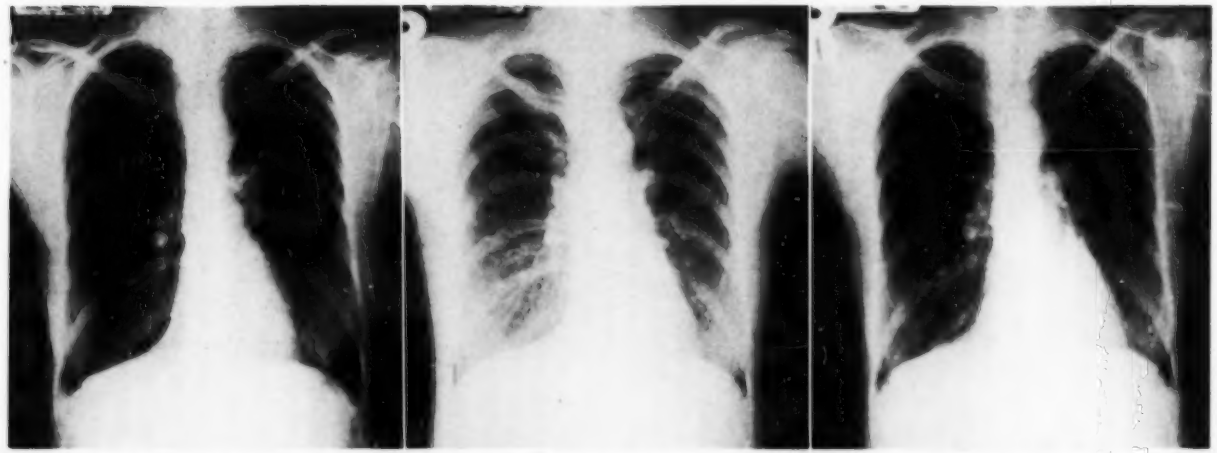

FIGURE 11D FIGURE 12D FIGURE 13D

11D, November 24, 1950: Sixty hours after Cortisone treatment started.
12D, November 24, 1950: Seventy-two hours after Cortisone treatment started.
13D, November 26, 1950: Fivt days after Cortisone treatment started, lungs clear.

vealed that this lesion was new and that the previous x-ray films showed a lesion in the right apex which had cleared, a lesion in the left first interspace which had cleared and a lesion in the left midfield which had been present two weeks before but which had now disappeared.

Blood count showed 23 per cent eosinophiles. A diagnosis of Loeffler's Syndrome was made.

She was hospitalized and given three blood transfusions and showed marked improvement almost immediately with a drop in the eosinophiles to less than one-half of one per cent. The asthmatic syndrome disappeared and she was discharged.

Allergy studies had been made which were essentially negative, except for a slight reaction to house dust. Stools were negative.

She remained well until the end of October, 1950, when she had another severe attack of asthma, began to lose weight and had loss of appetite. In November examination revealed a lesion in the left apex. Blood count showed 29 per cent eosinophiles.

She was again hospitalized for careful study and a series of x-ray films was taken and blood counts were performed every 12 hours to observe the rapidity of resolution of the lesion in relation to the eosinophile drop. On admission she was given 100 mg. of Cortisone, which was repeated every four hours for three doses. At the end of the 12 hours another x-ray film of the chest was taken and a blood count performed. The initial blood count showed 29 per cent eosinophiles and at the end of the 12 hours the count was 3 per cent. The x-ray shadow had not changed. She was then given 100 miligrams of Cortisone every 12 hours. The eosinophile count at the end of 24 hours was less than one half of one per cent but the x-ray film still showed no change. During the rest of the course of treatment, the eosinophiles never went above this figure and at the end of 60 hours the lesion had practically disappeared and at the end of four days was completely gone. She was symptom free within 24 hours after start of treatment.

The final x-ray film on the fifth day was completely clear. She was symptom free and was discharged from the hospital. There has been no recurrence since December, 1950.

Treatment and Prognosis

For many years there was no known treatment that altered the course of Loeffler's Syndrome. It was believed that the condition was allergic in character and antihistamines and various anti-allergic medications were tried. However, the course of the disease was not changed even though the symptoms may have been reduced.

In our series, the original cases were treated by injections of four minims of adrenalin every six hours merely as a means of holding down the bronchospasms with a hope that whatever bronchial occlusions might be present would not increase. Anti-histamines proved to be of little value. Adrenalin gave only slight symptomatic relief.

Antibiotics of various types were tried but it was noted that many of these cases did poorly with this therapy especially with penicillin and for that reason they frequently had to be discontinued.

In 1947, we noted that blood transfusions seemed to affect the course of the disease. The lesions cleared promptly, symptoms subsided and the eosinophile count dropped. This became our treatment of choice and the results were gratifying.

When Cortisone and ACTH were discovered, we used the former and were agreeably surprised at the response, both from a symptomatic stand-

point and from the x-ray film appearance. Many cases have since been treated with Cortisone and the results have been excellent. In some cases, both blood transfusions and Cortisone have been used and the results were gratifying.

The suggested method for blood transfusion is to give 500 cc. of while blood the first day and repeat the following day if the patient can tolerate that amount. If not, it is reduced in half. After 48 hours, another transfusion of either 250 cc. or 500 cc. is administered. Usually only three blood transfusions are required. We have repeated them every six or eight weeks thereafter in order to prevent recurrence of the disease. We can not explain the reason for the rapid response to blood transfusions but it has been suggested that possibly the blood contains elements similar to ACTH or Cortisone which changes the course of Loeffler's lesions.

In using Cortisone, we have given 100 mg. by injection every four hours for three doses, then 100 mg. every 12 hours until the lesion has cleared and the symptoms have subsided. The usual length of treatment has been up to five days. No ill effects have been encountered with the exception of one case where Cortisone had to be discontinued and blood transfusions employed. This patient had diabetes and apparently was unable to tolerate Cortisone.

Prognosis in Loeffler's Syndrome is very good. There have been no deaths directly attributed to this disease in our series.

Discussion

The 23 cases presented illustrate varied clinical and x-ray film pictures. Many of these cases do not fit Loeffler's description. A majority of the cases presented were symptomatic. Because of this variance in characteristics and symptomatology of similar types of cases, we feel that it is necessary to include all transitory or disappearing shadows with eosinophilia as cases of Loeffler's Syndrome. It is our conclusion that allergies are not basically important in the origin of this disease. Helminthiasis played a minor role in the cases reported herein.

The x-ray film appearance simulated many types of disease but most especially tuberculosis. Many of the x-ray shadows were atelectatic in appearance. Where the lesion was located in the lower lobes, the appearance was more of a patchy type and in those cases expectoration was a more prominent complaint than where the lesion was in the upper portion of the lung.

Cortisone has proved to be almost a specific in the treatment of Loeffler's Syndrome. Cases treated responded within a period of five days, the symptoms clearing within a maximum of 48 hours and the lesion clearing completely in five days or less. The suggested dosage is 100 mg. of Cortisone every four hours for three doses, then 100 mg. every 12 hours, hypodermically, to be continued until all symptoms have subsided and the lesion cleared on x-ray film. The usual length of treatment is only five days.

Before the advent of Cortisone and ACTH, blood transfusions were used with excellent results.

It is significant to note that the eosinophile count in these cases appeared to be at its highest percentage just prior to the beginning of clearing of the lesion. Usually the eosinophile count dropped rapidly and remained so as long as the lesion receeded. Prior to the development of new x-ray shadows or to recurrence of the same shadow, a slow progressive rise of the eosinophile count was noted.

There were no deaths directly attributable to this disease. The prognosis in all was good. Several had recurrences but were much more easily controlled when the diagnosis had been established.

SUMMARY

1) Twenty-three cases of Loeffler's Syndrome are reported.

2) Loeffler describes his cases as being asymptomatic. The majority of the cases reported herein had symptoms. In spite of the fact that symptoms were present, these must be included as Loeffler's Syndrome cases. If they are to be excluded, then a new terminology would have to be found for these symptomatic shifting or transitory lesions.

3) X-ray film characteristics are discussed.

4) Chief diagnostic characteristic was increase in the blood eosinophiles. It was noted that the highest percentage of blood eosinophiles occurred just before the lesion started to receed.

5) Major discrepancy noted was that Loeffler and others found helminthiasis present in practically all of their cases. In this series, a little over 10 per cent showed helminthiasis.

6) Treatment by regular injections of adrenalin hydrochloride showed no change in the x-ray shadow. Blood transfusions were then used and proved to be very successful, rapidly changing the course of the disease and clearing of the shadow. Cortisone has proved almost a specific in the treatment of Loeffler's Syndrome. Method used is described.

7) There were no fatalities. The prognosis in all cases of Loeffler's Syndrome is good.

RESUMEN

1) Se refieren 23 casos de síndrome de Loeffler.

2) Loeffler describió sus casos como asintomáticos. La mayoría de los casos aquí presentados, sí tenían síntomas. A pesar de esto, deben considerarse como casos de síndrome de Loeffler. Si tuviesen que excluirse entonces habría de crearse una nueva terminología para estas lesiones cambiantes o transitorias que presentan síntomas.

3) Las características radiológicas se discuten.

4) La característica diagnóstica más importante, es la eosinofilia en la sangre. Se notó la mayor proporción de eosinófilos precisamente antes de que la enfermedad empiece a ceder.

5) La mayor discrepancia consistió en que Loeffler y otros han encontrado la helmintiasis en prácticamente todos los casos. En esta serie un poco más de diez por ciento la presentaron.

6) El tratamiento con inyecciones regulares de clorhidrato de adrenalina, no mostró producir cambio en el aspecto radiológico. Las transfusiones

sanguíneas, fueron entonces usadas y se mostraron muy eficaces, al cambiar rápidamente la evolución de la enfermedad y al limpiar las manchas radiológicas. La cortisona se mostró casi especifica en el tratamiento de síndrome de Loeffler. El método usado se describe.

7) No hubo defunciones. El pronóstico en todos los casos de síndrome de Loeffler es bueno.

RESUME

1) L'auteur rapporte 23 cas de syndrome de Loeffler.

2) La description de Loeffler ne comporte pas de symptomatologie clinique. La majorité des cas rapportés dans la présente publication s'accompagnait de signes cliniques. Néanmoins, il semble qu'il faille les admettre dans le cadre du syndrome de Loeffler. Sinon, il y aurait lieu de trouver une nouvelle terminologie pour désigner ces manifestations.

3) Les caractéristiques radiologiques sont mises en discussion.

4) La caractéristique essentiel du diagnostic est l'accroissement de l'éosinophilie sanguine. L'auteur à constaté que le pourcentage le plus élevé de l'éosinophilie survient immédiatement avant la régression des lésions.

5) L'étude presente diverge surtout sur le fait que Loeffler et d'autres auteurs ont constaté que pratiquement tous les cas s'accompagnaient d'helminthiase. Cette constatation ne fut faite dans les cas considérés, que pour un peu plus d'un dixième d'entre eux.

6) Le traitement par des injections répétées d'adrénaline n'amena aucune modification des ombres radiologiques. Par contre des transfusions sanguines se montrèrent très efficaces, modifiant rapidement le cours de la maladie, et nettoyant l'ombre radiologique. La cortisone se montre un traitement presque spécifique du syndrome de Loeffler. L'auteur décrit sa technique d'utilisation.

7) Il n'y eut pas d'issue fatale. Le pronostic est bon dans tous les cas de syndrome de Loeffler.

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Pregnancy in Heart Disease

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Pregnancy is a normal physiological process producing an increased burden on the heart in the nature of an increase in its functional load. Pregnancy is well borne by the normal heart. The heart only fails in pregnancy when the heart itself is diseased or is not adequate to meet the functional load placed upon it. There is no pregnancy type of heart disease. When a cardiac patient becomes pregnant, her degree of compensation determine whether or not she will carry her pregnancy through to term.

The incidence of heart disease in pregnancy varies in various clinics, occurring in 1 to 4 per cent of the total number of patients seen. Under ordinary circumstances there is an increased blood volume in pregnancy, which, in turn, will increase the total metabolism of the body with the result that we will have a corresponding increase in oxygen consumption. This increase in consumption of oxygen varies a great deal in each individual, but probably is about 20 per cent above normal. Whether there is a corresponding increase in the basal metabolic rate is still debatable. Some observers feel that the essential basal metabolic rate does not increase in pregnancy while others feel that there may be an increase of 20 to 30 per cent. From the fifth to ninth month there is a gradual increase in cardiac output until it is estimated to be 50 per cent above normal, and during the last two or three weeks, there is a moderate fall in the output. The increased output is associated with a slight increase in the pulse rate. The increased work by the heart will be proportional to the cardiac output as well as to the arterial blood pressure. The blood pressure is not particularly elevated during pregnancy. There is an increase in the return of venous blood to the heart and as a result the cardiac output reflects this return. There is a slight increase in the acceleration of the circulation during the latter part of pregnancy. The blood volume increases during pregnancy and probably gets to be about 45 per cent above normal, and then diminishes to about 30 per cent above normal in the month before delivery. The plasma volume will also increase proportionately and there is an increase in cell volume. These changes that occur in the circulatory system are akin to those that occur with an arteriovenous fistula. In the placenta itself there is almost a direct communication between the arteries and the veins with a subsequent blood shunt from arterial to the venous side resulting in acceleration of blood flow with an increased venous return and a subsequent increase in cardiac output.

It is apparent that the circulating blood volume, increased as it is, and

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the increase in the venous return represent mechanisms which ordinarily are efficient in maintaining the normal circulatory balance but can be disadvantageous under certain circumstances. The diseased heart with its diminished functional reserve may be unable to maintain adequate cardiac output despite the fact that the blood volume has increased. The increase in blood volume will not be propelled normally as a result of the low reserve cardiac function. The result will be congestion of the lungs and viscera and signs and symptoms of congestive heart failure. Since these changes become greater after the fifth month and reach their height in the ninth lunar month, this intervening time is the time of challenge and danger to the pregnant patient with heart disease. If the patient carries through this period, the normal reduction of these phenomena brings the patient to labor in a fair degree of compensation. Heart failure occurring during labor or immediately following labor is rare. On the other hand, if heart failure is present when labor starts, there is some risk that the labor itself may manifest an increase in the myocardial insufficiency.

Symptoms Suggesting Heart Failure During Pregnancy

One must be aware of the fact that dyspnea is common in the last half of pregnancy and is due to the fact that the respiratory muscles increase their activity in order to maintain adequate circulation. It is the type of dyspnea that is seen in rapid weight gain. We must also be aware of the fact that the sighing syndrome is common in pregnancy. Palpitation and tachycardia are also common complaints in pregnancy. These symptoms are noted particularly after exertion, but, they seldom become an item of importance. The presence of edema is very common in the lower extremities. This association in pregnancy of edema and dyspnea may lead one to believe the patient is suffering from congestive heart failure. The cause of the edema in the lower extremities is probably the result of increased local venous pressure in the extremities, which, in turn, is augmented by the increased circulating blocd volume. The edema is not the result of heart failure and can be so determined by the absence of venous engorgement in the veins of the neck and also by the normal venous pressure. Cardiac enlargement may seem to be present if the apex pulse is displaced to the left and upward, but this is usually the result of an elevated diaphragm. An x-ray examination may also suggest the heart to be enlarged. One should recognize that in pregnancy, there is a tendency to overestimate the size of the heart. A systolic murmur may be heard particularly at the base of the heart, but a diastolic murmur is rarely heard unless disease is present. The presence of a high pulse pressure is not significant in the absence of an aortic valve defect. The electrocardiogram may normally reveal the effect of displacement of the heart.

The diagnosis of heart disease in pregnancy lies first in knowing that the patient had some type of cardiac lesion before she became pregnant. The symptoms of heart failure must be absolute and confirmed by physical examination and such laboratory procedures as are indicated. The types of heart disease seen in pregnancy will be similar to those found in the

general population. For example, there may be a congenital heart defect, a rheumatic heart defect, a luetic heart defect, hypertensive cardi-vascular disease, or coronary artery disease. Any of the other unusual types of heart disease may occur.

The prognosis is dependent on the functional classification of the patient's heart. Class I patient have no trouble; Class II have practically no trouble; Class II have some trouble; and of course, Class IV will have a great deal of difficulty.

The treatment of the patient who is pregnant and has heart disease is predicated upon the thesis that she should be treated for her heart disease as though she were not pregnant, and for her pregnancy as though heart disease did not exist. Such diagnostic procedures and therapy as the heart indicates should be given; and such obstetrical therapy as indicated should be rendered as though the patient were not a cardiac. Under no circumstances is it necessary to perform abortions or sterilizations in these patients, and above all, it is best to remember that there are no heart indications for any operative obstetrical procedures. The patient's treatment from the standpoint of obstetrics should be for those complications that arise in and around the obstetrical problem itself and not because of any problem that may arise by virtue of the heart disease.

To treat the pregnant cardiac patient bring her to term in the best state of compensation and permit her to deliver normally. The cardiac status should be treated as though the patient was not pregnant, and the obstetrical problem treated as though the patient did not have heart trouble. The watch-word throughout the period of pregnancy should be *conservatism*.

SUMMARY

There is little problem in the treatment of the patient who is pregnant and who suffers from heart disease. The physician should treat the heart disease as though the patient were not pregnant, and he should treat the pregnancy as though the patient did not have heart disease. In either condition the indications for treatment should be directed only to either the pregnancy or the heart disease. There is no heart disease which requires obstetrical interference. There is never an indication to interrupt a pregnancy or sterilize the patient because of heart disease.

RESUMEN

Ofrécese poco problema en el tratamiento de una paciente preñada, quien sufre de una enfermedad del corazón. Debe tratar el médico la enfermedad del corazón como si la paciente no estuviera preñada, y debe tratar la preñez como si la paciente no tuviera una enfermedad del corazón. En uno u otro caso las indicaciones para el tratamiento no deben dirigirse sine o a la preñez o a la enfermedad del corazón. No hay enfermedad del corazón alguna que requiera intervención obstétrica. No hay nunca indicación ni a interrumpir una preñez ni a esterilizar a una paciente a causa de la enfermedad del corazón.

RESUME

Le traitement de la femme qui est enceinte et qui souffre en même temps d'une maladie de coeur ne pose pas de grands problèmes. Le médecin devrait traiter la maladie de coeur comme si la malade n'était pas enceinte et il devrait traiter la grossesse comme si la femme n'avait pas une maladie de coeur. De toute façon les indications pour le traitement devraient porter soit sur la grossesse soit sur la maladie de coeur. Il n'y à pas de maladie de coeur qui exige une intervention de gynécologie. Il n'y aurait aucune raison d'arrêter le cours de la grossesse ou de stériliser la malade à cause d'une maladie de coeur.

The Clinical Syndrome of the So-Called Bronchial Adenomata*

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Some pathological non-tuberculous cases of the respiratory system of high clinical interest also to phtisiologists are described, as they may be easily mistaken for some forms of lung tuberculosis and also because of their peculiar and not well known clinical features.

Case 1: D.A.L., 31-year-old priest, had bronchopneumonia of the right lung in February 1945, from which he recovered after 10 days without any apparent sequel. In November of the same year, he had a sudden moderate hemoptysis, which lasted nearly a week as a simple bloody expectoration. He was feeling well, without fever, dyspnea or cyanosis and considered the occurrence of no importance, believing it to have been caused by the rupture of small vessels of the pharingo-oral cavity. He was put on hemostatic and calcium therapy and resumed his monastic habits, practising also in choral singing. He was perfectly well until February 4, when another hemoptoic episode occurred, with the same characters, namely a few days duration and moderate blood quantity.

He then had a medical examination including x-ray inspection of his chest, and tuberculosis of the right lung was diagnosed. He was admitted to Umberto I Sanatorium and two months afterwards, on May 25, 1947, transferred to Forlanini Institute.

Let us briefly dwell now on the anamnestic data. Before all, may an apparently common bronchopneumonia, followed, after nine months, by haemoptysis, be correlated to the diagnosis of tuberculosis made afterwards? It is not uncommon, for an exudative form of lung tuberculosis, namely an infiltrative form or a lobitis, to have a pseudo-influenzal or pneumonic onset, followed by a period of apparent respite, and, in a third stage, by a bronchial hemorrhage. The nine months respite is rather long, but not so seldom, especially under particular environmental conditions and organic response. The hemoptysis is rather to be considered as an isolated recurrent episode, not associated with fever or bronchopneumonic aspiration spreads of tuberculous material, as is often the case when it occurs during the evolutive course of a recent exudative process of lung tuberculosis. Is it then to be believed of non-tuberculous origin, consequent, for instance, to bronchiectatic bronchiolitis, echinococcus cyst or lung cancer? We should be careful in making such an inference, as clinical forms of lung tuberculosis with a typical hemoptoic evolution and no toxemic syndrome or spreads, are not at all seldom, as, for instance, chronic micronodular tuberculosis of the lung apex, or, even more, the so-called "apical abortive hemoptoic tuberculosis".

The next evolutive course of the illness seemed fully to confirm its specific tuberculous nature. The chest examination showed a tympanic hypophonesis of the right interscapulo-vertebral region and at the right posterior base, where a feeble and coarse vesicular breathing and a rale with small and middle inspiratory bubbles, more noticeable after coughing and with a stable sonorous character, were heard.

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The chest x-ray film taken at that time showed a thickening process in the right hilo-perihilar region, with areas of hyperclearness, on account of which, in spite of the Koch-negative sputum, both on direct examination and by the concentration method, the clinical diagnosis of infiltrate, subsequent to a right para-hilar pneumonia with incipient phtisiogenic evolution, was made. A right pneumothorax was performed on June 4, 1947. The pneumothorax was basilar selective and determined a collapse of the lower and middle lobes, which would have been even more complete, if it had not been limited by a diaphragmatic adhesion.

I had occasion to deal with the causes of this basilar selective pneumothorax, contrasting with the law of gravity in 1933 or 1934, in a polemic with Parodi, when I stated that the main genesis of this peculiar phenomenon was to be traced back to multiple potential stenoses of the tributary bronchi of the lobe, as made evident by the pneumothorax intervention, by which the lobe itself is being disengaged from the pleural surface, whereas Prof. Pigorini emphasized the weight of the infiltrated organ. The present case, remembering the above, is not merely of historical value, but also of considerable diagnostic importance.

Throughout 1947 and until April 1948, the patient was treated with right pneumothorax, which although being selective, did not yield the expected results and in particular did not influence either the hemoptysis, which recurred regularly about once every month, with the same early characteristic, or the general condition, which was gradually declining. In September 1947, in view of the low-placed location of the presumptive cavitation and of the presence of the diaphragmatic adhesion, which was directly transmitting the breathing traumatism of the diaphragm; a right phrenico-exeresis was considered advisable and performed.

In October, an exudative pleuritis occurred and the pneumothorax became

FIGURE 1, CASE 1

countraselective, causing an incomplete collapse of the upper lobe, so that it had to be abandoned in the following spring. In August, the diagnosis of lung tuberculosis, so far not yet confirmed, was bacterioscopically corroborated by the now Koch-positive sputum, firstly on culture and then on direct examination.

The patient was started on dihydrostreptomycin, penicillin and PAS therapy, which was continued through 1948 and in the first months of 1949, up to a total amount of 100 gm. streptomycin and 1,500 gm. PAS, resulting in general improvement, weight gain, more satisfactory biological tests, whilst objectively the pre-existent steto-acoustic findings (bronchial breathing with small and middle bubbling consonant rales in the right interscapulo-vertebral region) were unchanged.

In October 1948 we had a dramatic event, contrasting with the already demonstrated diagnosis of lung tuberculosis, namely the expectoration after a period of intermittent high fever, of copious, purulent and foetid sputum, upon which the temperature returned to normal and relative well-being followed. Radiologic examination on December 1, 1948, showed hyper-diaphanous, fibrotic, circled areas in the right parahilar region, suggesting coexistence of tuberculosis and bronchiectasis; bronchoscopic and bronchographic examination were therefore advised, but refused by the patient. The sputum was still Koch-positive on direct examination. A bronchography was performed only in December 1949, leading at last to the correct diagnosis: occlusion of the middle segment of the right stem bronchus at the bifurcation level of the middle dorsal bronchus, due to a hyperplastic endobronchial process, to be further corroborated by bronchoscopy. This was performed and confirmed the above findings, showing a big, ulcerated tumefaction, blocking the right stem bronchus below the upper lobar bronchus. The histological diagnosis obtained through the examination of biopsy specimens was that of an epithelial, small, atypical, round-cell tumor.

The suggested pulmonary resection was refused by the patient also in the following years; he is feeling fairly well, notwithstanding the recurrence of haemoptysis.

Let us now have in retrospect a critical survey of the diagnostic procedure and of the way by which the definitive diagnosis was finally reached, after fluctuating two years between several hypoteses, all supported, more or less, by objective data, namely: lung tuberculosis, polycistic bronchiectatis lower lobe, malignant lung tumor, benign lung tumor, correlated or not with bronchopulmonary tuberculosis.

How is the bronchopneumonic and haemoptoic early syndrome, which started in 1945 and recurred in 1947, to be interpreted? Was it to be considered as manifestation of an exudative lung tuberculosis, consequent to an ulcerated primary infiltration of the apex of the right lower lobe?

We have already noted, when drawing the clinical history, a few data not fully consistent with this diagnostic concept: the sputum repeatedly negative for tubercle bacilli for several years, notwithstanding the existence of small cavities in the parahilar region, the peculiar character of the recurrent haemoptysis without fever and without diffusion of the pathological process, the poor tolerance of the organism and the therapeutically unsuccessful selective pneumothorax. We cannot however deny the fact that after one year of hospitalization, the pneumothorax got infected with Koch bacilli, upon which a mild superficial bronchopneumonic infection occurred, which was successfully treated with streptomycin. It is not uncommon for hospitalized patients with bronchiectasis to get infected through daily contact with cases of open tuberculosis. This form is generally

characterized by a relative benign evolution, to be explained by the fact that the Koch bacillus does not find in the bronchoectatic cavitation a ground favorable to development, and has to withstand the counteracting influence of the other germs living in the same cavitation.

It would be more logical to infer, that an occasional exogenous superinfection occurred, unfortunately a not uncommon fact in hospitals for tuberculosis, where also a percentage of the staff is inevitably infected.

Are we to infer that on an early polycistic bronchoectatic syndrome an epithelial tumor was next implanted? This last inference is closely supported by the x-ray film and in particular by the tomographic findings of October 1948 (with honeycomb images) by the Koch-negative sputum at the onset, the recurrent foetid vomica-like expectoration, whereas the recurrent initial haemoptysis are features more characteristically correlated to bronchiectatic bronchiolitis than to manifest bronchiectasis. The typical anamnestical data of chronic bronchoblenorrhea of the common bronchiectatic forms, the objective signs of chronic bronchitis, of bronchial effusion, of clubbed fingers, etc., are however lacking.

In fact, it is since 1945 that the *clinical syndrome should have been corroborated by an endobronchial tumor of the middle segment of the right stem bronchus, which, during several years, assumed a typical pseudotuberculous evolution masked, even more, by the transitory appearance in the sputum of acid-fast bacilli, due to an exogenous superinfection.*

Having histologically ascertained the presence of an epitelial tumor with undifferentiated cells, we have now to deal with the fundamental question, if it is malignant or benign, if operable or not and, in the affirmative, with any chance of definitive success. In the present case, we have to consider also, besides the already mentioned contrasting findings, a last deep discrepancy between the atypical morphological finding, and consequently with all the features of an epitelial malignant neoplasm, and a clearly benign course of several years duration, with no regional or far-located metastasis, and not affecting the general condition. In effect, the tumor was relatively benign in its manifestations and course, although it was histologically simulating lung cancer, namely a *bronchial adenoma*, so called by the American authors and in particular by Chevalier Jackson, who lately described 40 cases from the Bronchoscopic Clinic of Philadelphia, covering a period of several years.

It is a bronchial tumor of not infrequent occurrence, with a characteristic clinical symptomatology, quite different from that of bronchial cancers, essentially connected with mechanical phenomena of partial or total occlusion of the stem bronchus, where it is located.

The last episode, which occurred in January 1952, is a foetid, vomitus-like expectoration, coinciding with the attempt made at another bronchoscopy. An exploratory puncture, performed in the right subscapular region, yielded 600 cc. pus, germ-free on bacteriological examination and on culture. After this, the patient feels well, is afebrile and still refuses to be operated upon.

If we look at the fine tomograph and bronchograph taken by Prof.

Pigorini, we shall have a full survey of the several pathological pictures, consistent with the bronchial tumor, in their succession.

Schematically, three stages are thus to be distinguished:

1) *The obstructive emphysema:* The primary increased translucency of areas located in the apex of the right lower lobe, were pseudocavities brought about by bullous emphysema, consequent to a partial blocking of the middle segment of the right stem bronchus. The mechanism of formation is quite evident: before reaching its full development, the bronchial tumor, which is often pedunculated, may work valve-like, namely, opening during the deep inspirations, when the bronchi expand, and letting in a little air, which reaches the lung area beyond the obstacle, and closing during the expiration phase. The air thus trapped in, is mostly absorbed, but, by and by, stagnation and consequently dilatation of the alveoli, occur, resulting in the rupture of the inter-alveolar and inter-lobular septa, with the subsequent development of large sized air cysts from obstructive emphysema. Sometimes this valve-like mechanism is felt by the patient himself, who complains as if his breathing were stopped in the expiratory phase, or as if something were flapping inside his chest. It may also cause objective acoustical symptoms of inspiratory hissing, or of metamorphosing breathing, namely, nearly silent in the first stage, and changing into amphoric breathing at the acme of the inspiration.

2) The stage of the *middle and lower lobe atelectasis*, which occurred transiently at the onset and in the middle period, when the total blocking was reached, also in the inspiratory phase, and the air supply to the area beyond the endobronchial tumor was stopped.

3) The third stage is that of the *"drowned lung,"* as in the present case. The endobronchial effusion, which may get infected by common germs, but mostly is transformed into purulent fluid, germ-free on ordinary examination, flows into the area beyond the obstacle and fills in the cysts caused by the obstructive emphysema. It may thus become large-sized as in the present case, and be mistaken for a saccular empyema. The lung or the lobe thus involved, may in fact be compared to a sponge plunged into a purulent fluid, from which the name "drowned lung". This stage inevitably leads to bronchiectasis or to a true obstructive abscess.

We are now in a position to conclude, with a relative certainty, that the patient is affected by a relatively benign, long standing bronchial tumor, which has passed through the three stages of obstructive emphysema, lower lobar atelectasis and drowned lung.

The *prognosis* might still be considered benign, if only the patient would follow our advice of submitting to total right pneumonectomy, which is the only adequate therapy under present conditions.

Case 2: O.M., 29-year-old employee. Nothing worth of note in her family and in her past personal anamnesis.

In March 1945, left bronchopneumonia complicated by exudative pleuritis and treated with common calcic therapy and with a thoracentesis yielding 300 cc. greenish-yellow exudate. Recovery in three months.

In April 1947, a few days after delivery, she complained of a lancinating pain

in the right hemithorax, with mild afternoon fever, cough and moderate mucous expectoration. She was therefore hospitalized in Trieste and dismissed after 45 days. The diagnosis of pleuritis, which, it would seem, was made then, was not confirmed by the exploratory puncture, which was negative.

In October 1947, a recrudescence of the catarrhal symptoms of the respiratory system occurred, accompanied by a broncho-asthmatic syndrome, remittent mild fever ranging to 37-38 degrees C. and profuse purulent expectoration. She had to be hospitalized once more, upon which her syndrome subsided under common symptomatic and penicillin therapy. But towards the end of the same year a fresh, more violent recrudescence occurred, with vomiting-like expectoration of large amounts of pus; an exploratory puncture at the base of the left hemithorax, revealed the presence of a purulent effusion, leading to the diagnosis of empyema with lung perforation, but following exploratory punctures were unsuccessful and the patient improved spontaneously and was dismissed.

In January 1948, there was a fourth episode of the same kind, but accompanied, this time, by *heavy haemoptysis*, intermittent fever and copious purulent sputum. A diagnosis of tuberculosis was made and the patient was sent to a middle height sanatorium, where she stayed seven months in fairly good condition.

In November 1948 she was transferred to the Forlanini Institute for surgical intervention. On entrance, her body weight was 62 kg.; a considerable retraction of the left hemithorax with disappearance of the respiratory mobility and of tactile vocal fremitus were found. The sound was clear above and below the scapular and the subclavian region, dull, with slight timpanitic echo over the

FIGURE 2, CASE 2

remaining lung area. Breath sounds were absent and no rales or friction were heard.

The x-ray film showed a marked opacity of the left lung, except at the apical region, where a hyperdiaphanous round-shaped image with an inner level was noted. The finding was grossly that of a fibrothorax with total left atelectasis.

The expectoration was negative for Koch-bacilli; Wassermann reaction negative; urine normal.

After 20 days' stay, the temperature rose intermittently to 38.5-39 degrees C., accompanied by lancinating pain in the left hemithorax. An exploratory puncture in the region of the left scapular angle yielded 100 cc. of thick gelatinous pus, which was partially substituted by air. In the following months, thoracocentesis was performed weekly and the patient was put on penicillin and streptomycin therapy, which was successful as to general and toxemic conditions. The culture of the empyema fluid was negative for Koch-bacilli and for other germs. The search for specific defense proteasis with tuberculous substratum was also negative. The tomographic examination repeatedly performed during 1949, showed, instead of a true empyema, several hydro-aerial sacks, some of which were confluent retrocardially and superdiaphragmatically, whilst a bigger one was located in the left upper lobe. The tomograph taken on June 7, 1949, disclosed further a blocking of the left stem bronchus, 2 cm. below the tracheal spur, due to an oval-shaped body, as confirmed by the bronchography, which was the typical image of the bottle stopper-like obstruction (Pigorini). The bronchoscopy showed the left stem bronchus totally filled in, 3 cm. off the branching, by a globose, hyperemic, smooth, soft, easily bleeding neoplasm measuring 10 cm. in diameter, rooted on the lateral bronchial wall.

The histological examination of the biopsy specimen led to the diagnosis of epithelial neoplasm with undifferentiated cells.

The suggested pneumonectomy was rejected by the patient, who, feeling well, preferred to leave the hospital.

After nearly one year, in the summer of 1950, she was re-admitted. During all that time she had complained only of chest pains and of a 3 kg. weight loss. As the local and general conditions were unchanged, the hypotesis of a malignant tumor logically was discarded. It was decided to submit the patient to a lung resection, which was performed at the Forlanini Institute in September 1950, quite successfully. The post-operative course was uneventful and the patient was dismissed in good health in March 1951. The last follow-up reports are good.

The removed lung was reduced to one third of its volume and was of much increased consistency, not containing air. The cut section revealed deep changes of the parenchyma, transformed into a compact mass, without air, highly sclerotic, with several hydro-aerial cystic sacks, containing a purulent gelatinous, reddish-yellow fluid. It is the classical finding of complete atelectasis with obstructive chronic pneumonia (picture of the so-called "drowned lung," according to American authors).

The left stem bronchus was obstructed by a small, smooth, elastic soft tumor, olive-sized, pedunculated on the lateral wall of the bronchus.

On account of its irregular ovoid shape and of the slight mobility allowed by the stem, the small tumor worked stopper-like to the main bronchus, which in its turn worked valve-like, namely allowing first the entry of the air, and henceforth the formation of an obstructive emphysema, and causing secondly a total atelectasis, with subsequent bronchial stagnation, as well as formation of several hydro-air cysts full of pus, due to the accumulation and to the changes occurring in the bronchial secretion beyond the blocking of the bronchus. The pulmonary cirrhosis is a logical consequence of the above.

The anatomo-pathological findings fully explained the symptomatology complained of by the patient.

The increasing bronchial obstruction is consistent with the feeling of constriction at the left hemithorax, due to the hindered entrance of the air into the lung; likewise are obstinate cough, recurrent haemoptysis, explained by the presence of the neoplasm near the cough area of the tracheal spur and by the frequent rupture of blood vessels of the tumoral mass.

The recurrent acute bronchitic syndrome coincided with the periods of highest stagnation of the bronchial secretion in the cysts caused by obstructive emphysema, and an effusion, at first greenish-yellow, then purulent, followed, simulating an empyema with scanty or no germs at all. Thus is the relative benignity of the affection explained. The asthma manifestations at the onset, were most likely also caused by reflexes with bronchospasm due to bronchial stenosis.

Case 3: D.C., 45-year-old, married, formerly stretcher-carrier. Nothing noteworthy in the family and in the past personal anamnesis. The patient was seized by the influenza pandemic in 1918, and recovered without complications.

In 1947 she underwent a bilateral hystero-oophorectomy, because of multiple myofibromatous uterus.

Married at the age of 24 years to an apparently healthy man, she had three pregnancies (one of which with premature delivery of a dead eight month old foetus).

In October 1950, onset of the symptomatology of the present clinical condition, namely: acute syndrome with remittent afternoon fever, ranging 38.5-39 degrees C., preceded by chills and followed by profuse sweat of about a fortnight duration, afterwards gradually subsiding and leaving a daily slight fever. At the same time she complained of diffuse osteo-muscular pains, asthenia, high-grade anorexia and, with regard to the respiratory system, lancinating pain, more marked at night, located at the right posterior base, with exertional dyspnea, persistent cough, productive of scanty muco-purulent secretion which was very tenacious. The patient felt also constriction in the right hemithorax, as if her breath were stopped both in the inspiratory and in the expiratory phase. She noticed also intermittently Galvagni's oral rale.

On examination, the sputum was Koch-negative and an x-ray film taken on October 2, 1950, suggested mediastinal pleuritis. But upon careful study of radiograph we found instead the features of actelectasis of the right lower lobe, with evident displacement of the trachea and the mediastinum to the right as well as a triangular opacity along the right heart border.

After one month of this symptomatology, she improved in November 1950, and was able to resume her normal activities.

The above symptomatology recurred once more in April 1951, with recrudescence of the respiratory symptoms and especially of the dyspnea, of pronounced cyanosis during the attacks of cough, productive of scanty muco-purulent sputum. The patient felt more and more markedly "difficult breathing" on the right, so as to be sometimes compelled to bend forward and nearly assume a Mohammedan posture, in order to eliminate the endobronchial secretion.

A diagnosis of pleuritis was made again and the patient was started on penicillin plus streptomycin, upon which the acute symptomatology disappeared.

She came under our observation in May 1951, and was in good general condition. No peripheral lymph modes were noted. Chest examination revealed a total retraction of the right hemithorax, more marked at the base, with lessening of the respiratory mobility and disappearance of the tactile and vocal fremitus. On percussion, there was tympanic hypophonesis of the lower, posterior and lateral half, with upper limit nearly horizontal. Throughout this area vesicular breathing was absent; on the remaining field, bronchial rales and big bubbles from concomitant chronic bronchitis were heard.

The cardiac area was enlarged 2 cm. to the right; the sounds were clear with some extrasystole. Small, rapid pulse, blood pressure 110/80.

No pathological findings on physical examination of the other organs. Sputum was negative for Koch bacilli.

A diagnosis was made of atelectasis of the right lower and middle lobes, secondary to presumptive stenosis of the right stem bronchus, with obvious signs of stagnation of the bronchial secretions. The necessary tomographic, bronchographic and bronchoscopic examinations were performed.

The tomograph in itself was most significant, showing at the hilus the presence of an ovular body, apparently located in the right stem bronchus and which was to be correlated, as disclosed by the following examinations, with the small-sized, endobronchial tumor. The bronchograph confirmed an obstruction of the middle section of the right stem bronchus, having the typical appearance of a bottle stopper-like stenosis, which differs, according to Pigorini, from the flute beak-shaped stenosis, commonly found in primary lung cancer. In this regard, Pigorini has made exhaustive bronchographic studies, which are shortly going to be published.

The bronchoscopy performed by Motta on June 5, 1951, showed: blunt, tracheal spur, scanty purulent secretions from the right stem bronchus, where, 2.5 cm. from the opening of the lobar bronchus, in the middle section, there is a small sized, smooth, soft, cyanotic red tumor, covered with scanty secretions, shifting with respiratory movements of the bronchus, not rigid and blocking totally the bronchus itself. The tumor was implanted posteriorly. Two small lentil sized specimens were excised for biopsy.

Prof. Pana's histological report revealed an epithelial tumor with undifferentiated cells of carcinoid type.

The patient followed our advice of surgical intervention and entered the Institute of Surgical Pathology, where on July 1951, right pneumonectomy was performed by Prof. Valdoni.

A small sized polypoid tumor of the middle section of the right stem bronchus was thus confirmed. Macroscopically the tumor, of the size of a small olive, did not extend beyond the bronchial walls. Obstructive pneumonia of the lower and middle lobe, which was atelectatic and full of pus, was present. The hilar lymph glands were enlarged, but on histological examination were not involved by the tumor, but only affected by chronic hyperplastic lymphadenitis.

The clinical anatomo-pathological picture was therefore that of a so-called bronchial adenoma.

The surgical intervention was well tolerated, with convalescence after a week.

Her general condition improved gradually and the manifestations of bronchial stagnation have permanently disappeared. In September 1951, however, she experienced a slight angina pectoris syndrome which did not occur any more.

At present, her x-ray film is the common one of pneumonectomized patients. A massive opacity of the right hemithorax, with slight displacement to this side, of the mediastinal organs. No functional cardio-vascular changes worth of note.

Case 4: B.G., 40-year-old, Ancona, finance petty officer. One sister died of lung tuberculosis in 1943. No illness worthy of note until December 1945, when he was seized by acute respiratory syndrome, interpreted first as influenza and then as right exudative pleuritis, as confirmed by exploratory puncture. Recovery within two months.

In February 1948, recurrence of the acute form with daily high intermittent fever up to 39.5 degrees C., preceded by chills and followed by profuse sweating, which lasted about a fortnight. He recovered only partly and has suffered since then from chronic muco-purulent bronchitis with periodical acute flare-up, especially in spring 1950, when he was admitted to the civil hospital in Ancona with the diagnosis of bronchiectasis of the right lung base. The sputum was always negative to tubercle bacilli. During his stay there, the patient had a sudden haemoptysis of moderate quantity. He was put under intensive antibiotic treat-

ment, namely penicillin-streptomycin therapy, with good results and no other acute bronchial attack occurred in the next 15 months.

On October 29, 1951, a sudden fresh haemoptysis occurred without apparent reason, afebrile, preceded by most intensive cough and cyanosis, after which he felt as if relieved from a weight and breathing more freely.

On January 23, 1952, he came to consult me, complaining of the usual broncho-blenorrhea, with daily 50-100 cc. expectoration, clearly bloody in the morning and changing into muco-purulent during the day, without foetor and negative for Koch bacilli. He complained also of a constriction at the base of the right hemithorax and of a hissing oral rale, especially in supine posture.

On objective chest examination, the patient, who had a brachitypic-macrosplanchnic constitution (body weight 82 kg.), presented a right posterior tympanitic dullness from the middle of the scapula downwards, extending to the axillary declivity and to the right mammarian area, with the upper border nearly horizontal. In this area the tactile vocal fremitus was lacking and breath sounds were very feeble, accompanied by creaking rales and by a group of moist, sonorous, small bubbling rales, located at the right base, not influenced by cough and which, according to his private physician, had been constant there for several years.

On careful auscultation above the dull area, especially in the right interscapular-vertebral area, an interesting acoustical feature was noted: when the patient was made to breathe long and deeply, the inspiration, silent in its first stage, was followed by a noise as if something were being detached, and changed into amphoric in the second stage.

On the left, the steto-acoustic findings were normal.

The spleen was slightly enlarged and of hard consistency. Examination of the other systems was negative.

Whilst at first, on the basis of anamnesis, I was thinking about the possibility of bronchiectatic bronchiolitis syndrome with hemoptoic evolution, later on, considering the above picture, I was led to the diagnosis of a manifest form of circumscribed bronchiectasis of the right lower lobe, secondary to *stenosis of the right stem bronchus, which had caused an actelectasis of the middle and lower lobes.*

Immediate radiographic and tomographic, bronchoscopic and bronchographic examinations were considered necessary.

The radiographic and the tomographic examinations have revealed evidence of a right basal pleuritis, with several hyperdiaphanous areas in the posterior strata, to be interpreted as bronchiectasis in atelectatic area, involving the right lower and middle lobes.

Bronchography confirmed the nearly total stenosis of the bronchus, like a bottle stopper, involving the middle section of the right stem bronchus. A small quantity of iodized oil could be made to pass the obstacle during deep inspiration and some cylindrical and saccular bronchiectasis, beyond the stenotic section was observed.

Bronchoscopy (Motta) showed the lumen of the middle section of the right stem bronchus, at the opening level of the mid-lobar branch, part of which is visible, is distorted, being nearly totally filled by a body implanted on the anterior wall of the bronchus, which is irregularly round-shaped, encephaloid, red colored, bleeding profusely at touching, shifting with every breathing movement, working like a valve. The parenchyma distal to the mass appears to be scantily areated and through the stenotic lumen a muco-purulent secretion is oozing. Two specimens were taken for biopsy.

The histological examination performed by Pana showed the presence of a bronchial carcinoid tumor, with several metaplasias of the bronchial epitelium (so-called adenoma).

A pulmonary resection, considered necessary on account of the co-existent bronchial adenoma and of the bilobar atelectasis with bronchiectasis, was performed in the Institute for Pathological Surgery by Prof. Valdoni, on March 21, 1952.

A considerable adhesive pachypleuritis was found, rendering necessary an ample extrapleural decollation, followed by the dissecting of the interlobar scissura, most long and difficult, and by the isolation of the lower pulmonary artery. The bronchus was severed about 1 cm. below the bifurcation of the midlobar bronchus, reaching the limit of the parietal adhesion of the adenoma. The right lower and middle lobes were then carefully isolated from their adhesion and excised and the upper lobe, filling nearly the whole chest cavity, was mobilized. The phrenic nerve running along the closure of the wall was not crushed. Drainage and suction of the considerable amount of blood oozing on account of the several dissected adhesions, were instituted.

On sectioning the two excised pulmonary lobes, the presence of a small tumor, the size of a cherry stone, adherent to the right middle segment of the bronchus, was brought to light. Besides the main body, small verruca-shaped formations of the same kind were noted. The peribronchial lymph nodes were enlarged, but not involved by metastasis. In the atelectatic lower and middle lobes, several cylindrical bronchiectasis full of pus are shown.

The present objective examination shows a right extrapleural hydro-pneumothorax, on the way of being spontaneously reabsorbed.

The upper lobe is gradually expanding and it is to be anticipated, that within a few months it will have taken a satisfactory vicarious functionality, and that except for pleuritic sequelae, no anatomical or functional signs of the severe illness will be left.

SUMMARY

In the opinion of the author, the etiological diagnosis of "bronchial adenoma" may be considered the true product of clinical reasoning and not only of histology, and is based on the following main data: (1) an initial, most openly pseudo-tuberculous syndrome or a masqued bronchiectatic syndrome with recurrent haemoptysis; (2) a symptomatology of bronchial occlusion, characteristic, but up to a certain point, of benign, endobronchial tumor with alternating or successive phases of obstructive emphysema, lobar and bilobar atelectasis, ending with the picture of the so-called "drowned lung"; (3) a characteristic very slow and fundamentally benign course of the tumor. The diagnosis must be confirmed, of course, by the tomography, bronchography and bronchoscopy. Histological biopsy findings are necessary, but their interpreting depend from a clinical and not only morphological standpoint. The author describes four cases of great clinical importance.

RESUMEN

En opinión del autor, el diagnóstico etiológico de "adenoma bronquial" puede ser considerado como un producto verdadero del razonamiento clínico y no sólo de la histología. Esta opinión se basa en lo siguiente: (1) Un síndrome abiertamente seudotuberculoso o un síndrome enmascarado de bronquiectasia con hemoptisis recurrente. (2) Una sintomatología de oclusión bronquial, característica, pero hasta cierto punto de tumor benigno endobronquial con fases alternantes de enfisema obstructivo, atelectasia lobar y bilobar, terminando con el cuadro del llamado "pulmón ahogado".

(3) Una evolución característica muy lenta y fundamentalmente benigna del tumor. El diagnóstico debe ser confirmado por la tomografía, la broncografía y la broncoscopia. Los hallazgos histológicos en la biopsia, son necesarios pero su interpretación depende de un punto de vista clínico y no sólo morfológico. El autor describe cuatro casos de gran importancia clínica.

RESUME

L'auteur émet l'opinion que le diagnostic étiologique de l'adénome bronchique doit être considére en fonction d'un raisonnement clinique et non seulement sur l'histologie. Il se base sur les éléments principaux suivants: (1) au début, un syndrome pseudo-tuberculeux ou simulant la bronchiectasie avec des hémoptysis récidivantes; (2) une symptomatologie d'occlusion bronchique caractéristique, mais jusqu'à un certain point de tumeur endobronchique bénigne, avec des phases alternatives d'emphysème obstructif, d' atélectasie lobaire ou bilobaire, se terminant par le tableau de ce que l'on à appelé le "poumon noyé"; (3) une évolution caractéristique, lente, et fondamentalement bénigne de la tumeur. Bien entendu, le diagnostic doit être confirmé par tomographies, bronchographie et bronchoscopie. Les constatations histologiques sont nécessaires, mais leur interprétation dépend d'un point de vue clinique et non uniquement morphologique. L'auteur discute quatre observations d'une grande importance clinique.

Pleural Adhesions, Their Incidence and Significance as Shown in Autopsies at the Los Angeles General Hospital, 1911-1951*

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The lungs, at birth, are covered by a thin, transparent, soft, glistening, moist and highly elastic membrance, the visceral pleura, which glides freely under the similar parietal pleura which lines the chest wall and diaphragm. In the course of time inhaled foreign materials and endogenous products may accumulate in the lymphatic network overlying the lung and may blacken the entire lung surface and its substance. Injury to the pleura results in proliferation of connective tissue, with thickening, opacity, and loss of elasticity of the membrance. Damage to the lining cells of the pleura may lead to the formation of permanent adhesions between the visceral and parietal pleurae.

Acute and chronic pleural lesions are usually associated with disease of the underlying lung. They are most often due to tuberculosis, but may accompany or follow pneumonia, lung abscess, or other inflammatory conditions in the chest. Pneumonia is about as common as tuberculosis as a cause of death and has a similar hospital case fatality rate. The incidence of empyema and other pleural complications following it has been greatly reduced by antibiotic and other chemotherapy, but how often healed pneumonia leaves pleural adhesions is not known. Pleural effusion from cardiac decompensation may resorb without adhesion formation, but traumatic pleuritis, or hemothorax, is usually followed by pleural symphysis.

More than 0.2 per cent of all deaths in the United States were ascribed to pleurisy half a century ago, but less than 0.02 per cent were so recorded during the past few years and even these are of dubious significance. Pleurisy is present more often among clinical diagnoses in general hospitals than on death certificates. It was reported in from 1 to 3 per cent of all patients admitted to the Massachusetts General Hospital,[1] the Pennsylvania Hospital and the John Hopkins Hospital at the beginning of the century and was recorded in 1.5 per cent of the more than a million patients treated and in 4 per cent of the 112,000 who died at the Los Angeles General Hospital during the past 30 years.[2]

Experimentally pleural adhesions have been produced in man and in animals by the intrapleural injection of blood, talc and other agents or by

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direct surgical intervention and packing.[3] Guinea pigs and rabbits infected with tuberculosis by the aerogenous or intravenous routes as well as those infected by direct intrapleural injection may also develop pleural involvement, but this is not often observed after the usual subcutaneous or intraperitoneal route of infection.

Tuberculous infection in man is often followed by pleural involvement, with resultant adhesions. Since primary foci are apt to be peripheral, the lymphatic drainage by way of the pleural lymphatics before eventually emptying into the hilar lymph nodes gives ample opportunity for pleural involvement.[4] Pleurisy, usually with effusion, has been reported in about 20 per cent of all persons who have a positive tuberculin test, within a few years of the primary infection. This is undoubtedly an understatement of the true incidence, as the diagnosis is apt to be missed unless symptoms are complained of and investigated, or x-ray films are taken at the exact time that the effusion is present.

Even in a tuberculosis sanatorium, where pleurisy is especially inquired into as a diagnostic sign, it is incompletely diagnosed and reported. Among more than 20,000 patients treated at the Olive View Sanatorium between 1920 and 1950, 22 per cent reported a pleuritic type of onset, and 58 per cent mentioned an attack of pleurisy before admission, while only 5 per cent definitely denied any such symptoms, at any time.[5] It is probable that few cases of clinically manifest reinfection type pulmonary tuberculosis completely escape pleural complications.

Pleural adhesions between the visceral and parietal pleura have been observed so often in adult autopsies that pathologists often describe them without including them among the diagnoses or attaching any special significance to them.[6] Such adhesions may be faint or firm, fibrinous or fibrous, thin or thick, soft or calcific, and may vary in extent from fine or coarse, thread, string cord band or cylindrical adhesions localized or extensive discrete or diffuse symphysis with obliteration of the pleural space. Pleural adhesions may be localized in any part of the chest cavity, but are often found posteriorly in the superior part of the chest, near the mediastinum, or along the interlobar fissures. Adhesions following hemothorax, trauma or simple effusion may be basal, or diaphragmatic.

The frequency of occurrence of adhesions between the visceral and parietal pleura in large unselected series of autopsies have been reported by a number of workers to vary from about 40 to 80 per cent.[7-10] Others have merely emphasized their great frequency, or indicated that they were usually present without giving specific figures. More detailed tabulation of the data shows that the most important variable affecting the incidence of adhesions is the age of the persons autopsied.[11] Infants rarely show pleural adhesions, old persons rarely lack them, and the incidence of adhesions in general increase with the increased age of the subjects. In groups of similar age distribution there are generally much more adhesions among men than among women, and among white patients than among the colored races, and among urban as compared with rural residents. Moreover, series studies in more recent years, at least in this country, show

a lower incidence of adhesions, especially in the lower ages, than those reported a generation or more ago.

In order to learn more regarding the condition of the pleura, the actual descriptions recorded in the protocols of a representative sample of the 44,000 autopsies performed in the Los Angeles General Hospital from 1911 to 1951 were reexamined. For this purpose 28 different groups of 100 consecutive autopsies were selected and each protocol was reviewed individually to determine what statements it contained regarding the condition of the pleura and the presence and absence of adhesions on the two sides. The pleura was specifically mentioned in more than 90 per cent of the cases, and the small group in which such information was missing consisted chiefly of infants, or in autopsies performed in the earlier years, when the descriptions were much briefer and apt to be incomplete.

The normal pleura was usually described with the words smooth, shiny, glistening, free, normal, unchanged, negative, or no lesions, or without adhesions. Pathological lesions such as pleural fluid, nodules, thickening, or other changes in the pleura or pleural space were sometimes noted without mention as to the presence or absence of adhesions. By far the most frequent lesion noted, however, consisted of adhesions, which were bilateral almost as often as unilateral, and were often described as complete, obliterative, entire, or leaving no free space.[12,13] Altogether, two thirds of the protocols examined described some pathological change in the pleura, although in only a quarter of the cases were such lesions included in the diagnostic summary. Adhesions were specifically recorded in nearly 60 per cent of all the autopsies in which information on this point was given. There were consistent differences, however, in the frequency of occurrence of pleural adhesions in different demographic groups.

Great differences in the occurrence of adhesions were noted on separating the frequencies on the basis of age. Only 11 per cent of those under 20 years of age had adhesions, as compared with 66 per cent above that age. There

PERCENTAGE OF AUTOPSIES SHOWING PLEURAL ADHESIONS
Los Angeles General Hospital, 1911-1950

	Tuberculosis Not Diagnosed	Tuberculosis Diagnosed	Total
Total	52	88	59
Age: Under 20	10	60	11
20 to 39	60	90	66
40 and over	60	89	65
Male	58	92	61
Female	40	70	45
White	53	89	60
Negro	50	72	57
1911 1930	61	89	72
1931-1950	50	85	54

were more adhesions in males than in females, at all age periods, in all of the time periods and races studied. Adhesions were also more frequent in white persons than in negroes, in all sex, age, and time series studied. The frequency of adhesions in the successive series of autopsies diminished in more recent years, especially in the younger age groups. In the earlier years more than two-thirds of all cases showed adhesions, more recently only about half presented such findings.

The most striking differences in the occurrence of adhesions were evident on separating the data for the cases with an autopsy diagnosis of tuberculosis from those in which tuberculous lesions were not reported. Adhesions were described in 85 per cent of 505 tuberculous cases, and an additional 5 per cent had fluid, nodules, or other pleural lesions which might have been expected to leave adhesions if the patient had survived long enough.[14] Thus only 10 per cent of these autopsies in which tuberculous lesions were recognized had normal pleuras, as compared with nearly half of the autopsies in which tuberculous lesions were not diagnosed. Among the patients whose primary cause of death was tuberculosis, more than 92 per cent had adhesions or other lesions of the pleura, while of the patients who had tuberculous lesions but died primarily of some other condition, 88 per cent showed such involvement.

Among all these autopsies, as has been previously reported,[15] tuberculous lesions were found more often in males than in females, more in older patients than in younger ones, and more in earlier years than in more recent years. The same is true of the incidence of pleural adhesions. It is plausible to infer that the incidence of such adhesions, which are so much more frequent in the presence of known tuberculosis than in its absence, may, in the cases of which the tuberculosis is not reported, actually reflect the effect of a tuberculous infection which has not been recognized.

Among the entire series, tuberculosis was less frequent in white than in other races, but the reverse is true of the presence of adhesions. This is true even though among all races the effect of age, sex, and chronologic time of autopsy appear similar. In each age, sex, and time series, and both in those with and without diagnosed tuberculous lesions, the incidence of adhesions was lower in negroes than in whites.

The frequency of adhesions in persons with positive tuberculin tests but who do not have gross tuberculous lesions at autopsy can not be stated with assurance, since no series is known in which the tuberculin sensitivity has been correlated with the autopsy findings. These persons may have less than the 90 per cent incidence of adhesions seen with fatal or nonfatal gross tuberculous lesions at autopsy, but they would probably have much more than the 50 per cent observed in the general autopsy population without gross tuberculous lesions. The incidence of positive tuberculin tests in the community, according to the fragmentary data available, rises with age and has been increasing more slowly in recent years, so that the rates are relatively much higher in the older groups. A similar relationship is seen for the incidence of adhesions at autopsy. In fact, it would seem that the actual incidence of adhesions at autopsy is not much different than might

be expected to be the incidence of positive tuberculin tests in the same groups.

Although tuberculin skin tests have given abundant information regarding the incidence of tuberculous infection in the younger population of various countries, especially since the inauguration of the world wide BCG vaccination campaign, relatively little information is available regarding such infection in older age groups. In the past, as in countries where the incidence of the infection is extremely high, almost universal infection of urban adults may be assumed. In the future and in places where tuberculosis already is coming under control, the decline in infection which is already conspicuous in the younger ages may be expected to apply to the older population also. Since the presence of pleural adhesions observable at autopsy appears to be closely related to the history of tuberculous infection, the determination of this incidence may be an added aid in the evaluation of the success of the tuberculosis control program.

SUMMARY

Adhesions between the visceral and the parietal pleurae have been observed in the majority of adult autopsies. They are more frequent in older males, and white persons, and their incidence has been decreasing, especially in the younger age groups, in recent years. They are present in more than 90 per cent of all persons dying of tuberculosis, and in nearly as high a proportion of persons with gross tuberculous lesions who die of other causes. Although adhesions may occur as a result of non-tuberculous causes, their incidence so closely parallels the incidence of tuberculous infection that they may be utilized as an indication of the efficacy of tuberculosis control measures.

RESUMEN

En la mayoría de las autopsias de adultos, se han encontrado adherencias entre las pleural visceral y parietal. Son más frecuentes en los hombres de edad y de raza blanca y su frecuencia ha venido disminuyendo en los últimos años, especialmente entre los jóvenes. Se encuentran en más del noventa por ciento de los que mueren de tuberculosis y casi en la misma proporción en las personas que teniendo lesiones grandes de tuberculosis, mueren por otras causas. Aunque las adherencias pueden producirse por otras causas aparte de la tuberculosis, su frecuencia guarda una relación tan estrecha con la infección tuberculosa que puede estimarse como una indicación utilizable para determinar la eficacia de las medidas de dominio de la enfermedad.

RESUME

Des adhérences entre les plèvres viscérale et pariétale ont été observées dans la majorité des autopsies d'adultes. Elles sont plus fréquentes chez les individus de sexe masculin, d'un certain âge, et chez les blancs, et leur fréquence va en décroissant ces dernières années, surtout chez les individus plus jeunes. On les trouve dans plus de 90% des individus mourant de

tuberculose, et dans une proportion presque aussi élevée chez des individus qui meurent pour d'autres causes, mais qu'on a trouvé porteurs de lésions macroscopiques de tuberculose.

Bien que les adhérences peuvent apparaitre sans être d'origine tuberculeuse, leur fréquence est si intimement liée à la fréquence de l'infection tuberculeuse qu'on peut les utiliser pour indiquer l'efficacité des mesures de contrôle en tuberculose.

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Bronchiectasis Due to Aspergilloma*

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A special form of pulmonary mycosis, characterized from an anatomical point of view, by the presence of a limited mycelian tumor of aspergillus origin in a distended bronchus, is herewith reported.

The accumulation of mycelium filaments forms a mass which takes the aspect and the color of a truffle. The lesion is solitary and this differentiates it from the diffuse forms of broncho-pulmonary aspergillosis. The clinical picture is marked by repeated hemorrhages and there is a typical x-ray picture. We are reporting three operated cases.

In our first case, observed with Warnery and Lespinasse, mycelium filaments were identified in the patient's sputum, but we did not dare make a definite diagnosis of mycosis. In our second case, diagnosis had not been made before operation. In our third case, observed with San Emeterio, it was made. This enabled us to perform the only logical procedure—segmental resection of the involved portion.

Four cases have been reported by other authors which we have grouped together to present this new and rare pathological entity. This report is based upon nine case histories.

Aspergillus fumigatus has been identified four times; an aspergillus was observed three times and an aspergillus like organism, once. In two cases there was a strong presumption in favor of an aspergillus by microscopic examination and comparison with identified cases although no culture was done.

Case 1: M.M., age 39, was reported to have had pleuritis on the right side with a "lesion" on the same side 15 years previously. In 1946 and 1947 minor pulmonary hemorrhages occurred. In March 1948, an abnormal right sub-hilar shadow was seen which was interpreted as a new tuberculous exacerbation and the patient was sent to a sanatorium for the fifth time. Tubercle bacilli, however, were not found in the sputum. The x-ray film caused attention because of the following details:

A perfectly round, uniform, not very dense opacity, the size of a half-dollar was observed in the right paramediastinal region. Its upper outline was topped by a highlight in the shape of a clear, sharp and thin crescent. This appeared to be a pulmonary cavity containing an opacity. There was no reaction in the surrounding areas and the remainder of the lung was normal. The shadow did not increase in size between April and October 1948. Such a peculiar picture cast great doubt on the existence of tuberculosis.

Among the laboratory examinations, in addition to the negative sputum, there was blood eosinophilia of 7 per cent and a negative blood Wassermann. The Casoni reaction could not be carried out for hydatid cyst. The provisional diagnosis was hydatid cyst with embryonic cyst or intrapulmonary aneurysm considered as possibilities. Exploratory surgery was decided upon. This was done on October 21, 1948, by the transpectoral anterior approach, resecting the second and third ribs.

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The pleura was found adherent. Both the pleura and the lung were heavily vascularized. On incision of the lung with the diathermy knife, a large cavity, with no particular membrane, was entered. This was filled with a substance similar to mastic. The pulmonary parenchyma which was incised was extremely hemorrhagic but not solid or sclerotic and hemostatic sutures were necessary all around the pulmonary opening. The cavity was marsupialized. Death occurred 33 hours following the operation from an undetermined cause.

The histological examination of the solid area, removed during the operation, showed "no organized tissue" but a "coating of ramified filaments" septated, with thin walls, the diameter varying from 2.5 mu. to 8.5 mu. There were numerous bulges at the periphery of the mass (diameter 15 mu.). In various places, an inflammatory polynuclear reaction was connected with the mycelium mass.

Case 2: J.D., male, age 42, gave a history of hemoptyses without fever and without evidence of infection. Three of four such hemoptyses had occurred during the 20 years prior to 1938; two such episodes occurring at shorter intervals brought him to the sanatorium. From 1939 to 1944, he was admitted three times during which gold salts, left pneumothorax and left phrenectomy were the treatments used.

During these five years, a great many bacteriological studies were made but on only one occasion were tubercle bacilli reported. In 1942, he began to expectorate purulent sputum in which no bacteria were found. This expectoration continued. In 1944, he suffered repeated hemoptyses and was institutionalized for the fourth time. Numerous x-ray films, from 1939 to 1944 showed exactly the same shadows: a large dense area under the left clavicle; its upper half surmounted by a highlight in the form of a thin, clear crescent, itself limited peripherally by a thin line. The pulmonary parenchyma was normal up to the contact with this opacity. On the other hand, bronchial dilatation as demonstrated by iodized oil, existed in the base. The iodized oil did not penetrate the cavity containing the opaque mass.

A diagnosis of mycosis was considered. Examination of the sputum in April

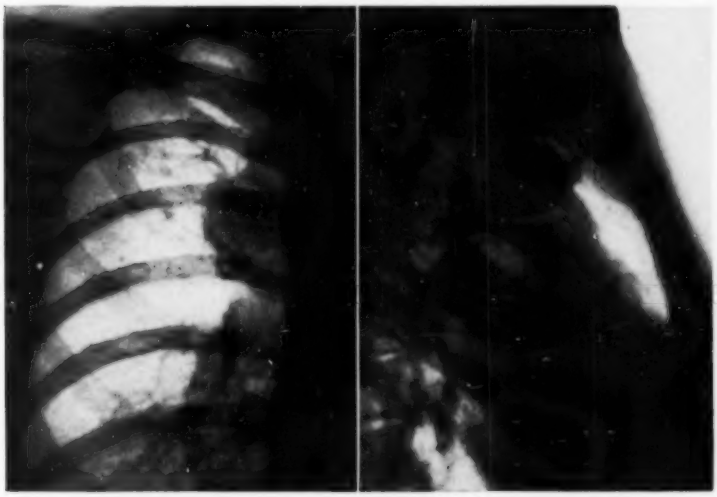

FIGURE 1 FIGURE 2

Figure 1, Case 1: X-ray film of chest PA demonstrating lesion just below clavicle showing crescentic shaped highlight in the upper portion. — *Figure 2, Case 1:* Lateral view of same patient demonstrating density and superimposed highlight.

1944, indicated the presence of abundant mycelia but circumstances did not permit identification. Iodide treatment provoked new hemoptyses without producing any change in the x-ray findings. Benign tumor or hydatid cyst were also considered. The Casoni reaction was positive, but blood eosinophilia was not observed.

Bronchoscopy was performed in April 1945. A little edema of the left upper lobe bronchus was the only abnormal finding. Pneumonotomy was performed on April 17, 1945, by transpectoral anterior approach. The pleura was found to be adherent. The lung was opened with the diathermy knife. A cavity, the size of a plum, filled with a pasty brownish and odorless material was found. The internal wall of this cavity was regular, pink and granular. The draining bronchus had a large lumen, opened at the superior-posterior and also at the inferior portion. The inferior half of the cavity wall was resected. The incision of the pulmonary tissue was hemorrhagic. The internal wall was completely cauterized with the diathermy knife. Two drains were left in and it was kept open.

The immediate postoperative course was complicated by two copious hemoptyses. The bronchi could be seen in the cavity wall and were cauterized with silver nitrate and healed within four weeks. The wound granulated without any suppuration and he was discharged.

Histological examination of the cavity: "True cyst with an epithelial cylindrical lining of the bronchial type with the appearance of squamous metaplasia. The presence of numerous excretory ducts of a bronchial type with cylindrical mucous

FIGURE 3, CASE 2: PA view, March 13, 1945, showing large density with this crescentic shaped highlight in upper portion. Contrast media shows bronchiectatic dilitations at base.

membrane (positive muci-carmin), pulmonary atelectasis and lymphoid masses in the wall of the cyst. It had the aspect of a true congenital malformation and of a true pulmonary cyst."

In December 1950, five and one-half years after the operation, he was in good condition but had had repeated non-bacillary hemoptyses. We believed, as there was no abnormal x-ray finding in the operated area, that these were due to the bronchial dilatations at the left base which were observed by bronchography prior to the operation. He was in good condition in June 1951, and was able to work.

Case 3: M.L., male, age 35, had had right pneumothorax 10 years previously because of repeated hemoptyses although no bacteria were found in his sputum. Although pneumothorax had a favorable effect upon the hemorrhagic episodes, it was abandoned after two and one-half years. Six years ago, he went through a series of slight daily hemoptyses which were improved by lying down. No alteration of his general condition was observed. Fourteen months ago, he had a serious hemoptysis and another two weeks previously. He remained in good general condition and was afebrile.

X-ray film revealed four or five nodules of a sclerotic type in the right apex. A round image of medium opacity was seen behind the left clavicle with a thin clear crescent-shaped zone at its top.

No tubercle bacilli were found in the sputum, but a mycelium was reported. Bronchoscopy showed only a little blood coming from the left main bronchus.

FIGURE 4, CASE 3: Specimen of resected left apical dorsal segment showing the large bronchiectatic cavity and the mass of mycelium removed from it.

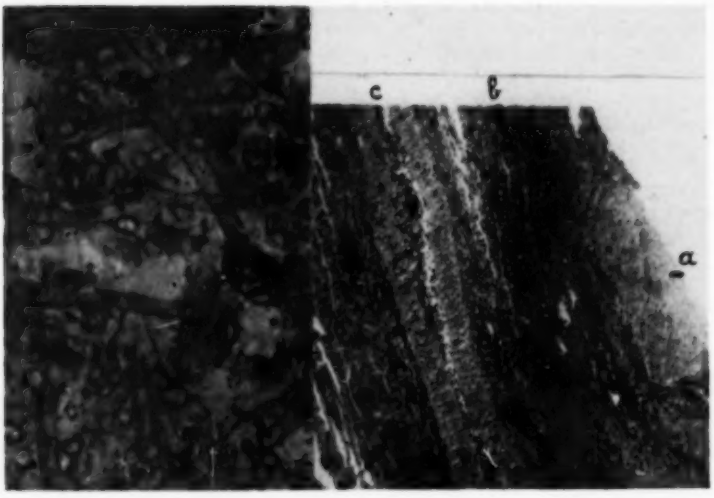

FIGURE 5 FIGURE 6

Figure 5, Case 3: Photomicrograph of the central mass showing same shaped mycelium filaments in 500x.—*Figure 6, Case 3:* Photomicrograph showing bronchiectatic wall. (A) Fregment of central mycelian mass resting directly on damaged bronchial epithelium.—(B) Cellular infiltration of collapsed pulmonary tissue.—(C) Compressed bronchus containing red blood cells and polynuclears 80x.

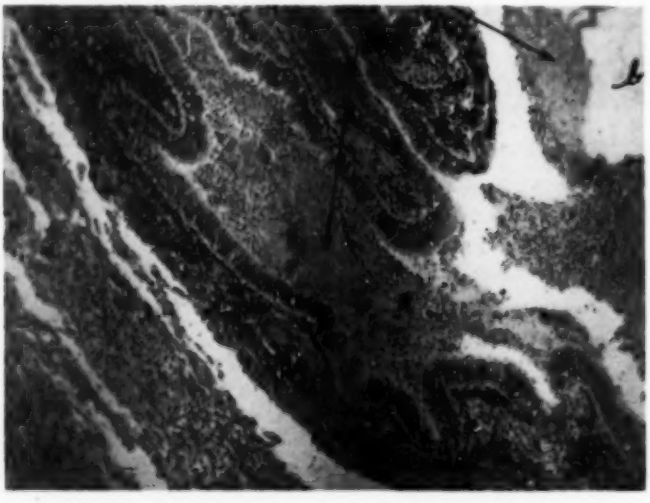

FIGURE 7, CASE 3: Photomicrograph of section of bronchus showing two masses of fungi. In the middle, a hemorrhagic reaction in which a dilated bronchus and the other in a flattened bronchus 80x.

Antibiotic therapy consisting of 20 million units of penicillin and streptomycin (30 gr.) had no effect.

In short, this was a case where the patient had had repeated hemoptyses for 10 years during which no tubercle bacilli were recovered from his sputum. X-ray films showed a peculiar shape similar to the image observed in the two preceding cases. We diagnosed an intrabronchial mycetoma, and consequently assumed that resection would be necessary.

Resection of the apical and dorsal segments of the left upper lobe revealed a round mass in this area (segments one and two).

After the operation, this specimen was aspirated aseptically and the material seeded in several glucose tubes and Petri dishes. Various saprophyte fungus strains developed in the culture at ordinary temperatures. Only one colony of aspergillus was observed at 37 degrees C. which was pathogenic for the rabbit by intravenous injection of a suspension of spores.

The surgical specimen contained an enormously dilated bronchus which contained a pasty sequestrum. Sections were made in the middle of the tissue which filled the extremely dilated lumen of the bronchus. This tissue was composed of fan shaped, thin-walled filaments with a diameter varying from 2.5 mu. and 8.5 mu. showing frequent swellings of the periphery where they reached a diameter of 15 mu. We did not observe spores of the fungus or any substance between the filaments. The filaments were optically empty except for the external part of the mass where mycelian contents were stained. We observed small hemorrhages with a slight cellular multinuclear reaction at the periphery of the mycelian mass.

Sections were made in the bronchial wall and in the subjacent pulmonary tissue, where the mycelian mass was fixed to the bronchus. Fragments of the central mass remained fixed on the bronchial wall and we noticed that this mass was either directly in contact with the epithelium or separated from it by a polynuclear exudate. The fungus did not penetrate the bronchial epithelium although the latter was altered. Besides the central mycelian mass, several heaps of the fungus were observed in an effusion of blood in a flattened bronchus connected to the dilated bronchus.

The pulmonary tissue was seriously altered. In the whole region contiguous to the dilated bronchus and in some places deep in the pulmonary parenchyma, we observed a cellular infiltration where plasmocytes were most numerous and where large mononuclears, mastocytes and polynuclear cells were also visible. Hemorrhagic areas with groups of polynuclears were seen. Eosinophiles and giant cells were not found.

Conclusion: A heap of filaments entangled with fungus, surrounded by polynuclear, cellular reaction has only been observed in mycetoma. Therefore, we felt that this lesion may be considered mycetoma. Yet the latter differs from true mycetoma by the presence of a single "grain" of an unusual volume, by the localization of the lesion and finally by the incomplete peripheral reaction. However, the reaction of bronchial tissue near it seems to indicate a certain toxic effect of the fungus. The presence of plasmocytes confirms the chronic type of the disease.

The isolation by culture of aspergillus fumigatus would be necessary to indicate this is really the agent involved. However, we could not make this definite identification from the appearance of the fungus on histological section.

The following six cases are here compared with our three.

Case 4 (reported by Dévé): Male, age 25, in apparent good health but had had repeated hemoptyses at irregular intervals. There was no other clinical manifestation except for accentuated clubbing of the fingers and toes. Tubercle bacilli were never observed in his sputum. X-ray film showed an "ovoid shadow" rather regular and strictly limited, located in the center of the lower lobe of the right lung, extending from the fourth to the sixth rib, posteriorly, surrounded by an

FIGURE 8

FIGURE 9

Figure 8, Case 8: PA x-ray film of chest showing shadow behind clavicle demonstrating typical crescentic highlight.—*Figure 9, Case 9:* Tomograph of similar case demonstrating the structure producing the highlight.

FIGURE 10, CASE 9: Photomicrograph of arterio contiguous to fungus demonstrating the interruption of the vascular wall which produces hemoptysis 30x.

"aerial tegmentum" in the upper half. Tests for echinococcosis were negative.

Deep x-ray treatment was administered to no avail. An "hemostatic" pneumothorax had no effect. Finally, exploratory thoracotomy was performed. The post mortem examination showed a large cavity with walls lined with bronchial epithelium containing an ovoid mass, the size of a hen's egg. This was formed by a "dense mycelious coating," due to a fungus of the aspergillus group.

Case 5 (reported by Metras and Thomas): Male, age 40, who for six years had suffered from a fetid, sometimes bloody abundant chronic bronchorrhea. X-ray film showed a "sequestrum". The histological examination (Dr. Pourcine) revealed a cavity with a bronchial-type wall and a foreign body the size of a walnut composed of a mycelious heap of an aspergillus type adhering to the wall without penetrating it.

Case 6 (reported by Gerstl, Weidman and Newman): This is similar to the other, having repeated hemoptyses for 11 years. X-ray examination showed a rounded opacity without any "aerial tegmentum"; it increased under observation and was not influenced by deep x-ray treatment. Lobectomy was successfully performed. A cavity of bronchial origin was found filled with a brownish-purple mass formed by mycelium and spores of a fungus resembling aspergillus.

Case 7 (reported by Yesner and Hurwitz): Male, age 35, on a routine examination, an opacity of the left lung was found. Four months before, during an influenza attack, he expectorated red blood. No tubercle bacilli were found in the sputum on six examinations. Bronchoscopy revealed no abnormality. X-ray film showed an ovoid opacity, well limited, in the apex of the inferior left lobe. Chronic abscess, tuberculoma and bronchogenic carcinoma were considered. Left lobectomy was performed and culture indicated the presence of aspergillus fumigatus.

Case 8 (reported by Orie, unpublished): Male, age 46, had a history of frequent bloody expectoration for six years. No tubercle bacilli were found. Bronchoscopy was normal. X-ray film showed a shadow in the right upper lobe identical in every way to the one described above. Very small bronchiectases were observed in the left lower lobe. Lobectomy was performed in November 1950. At the opening of the specimen, a bronchial cavity filled with a pasty spherical mass was found. The culture was identified as aspergillus fumigatus.

Case 9 (reported by Kraan and Orie): Female, age 56, had a history of cough for 20 years without hemoptysis. No tubercle bacilli were found in the sputum. X-ray films and tomographies showed a shadow in the apex of the right upper lobe similar to that described above. An exploratory puncture was performed in the chest. In nine culture tubes out of 10, a fungus grew identified as aspergillus fumigatus.

Clinical Discussion

From these observations we believe we are able to correlate a clinical picture which may be diagnostic. Hemoptyses are solitary, scanty and recurrent. In at least two (Dévé's and our third case) hemoptysis showed the peculiarity of being affected by position of the patient. Tubercle bacilli are not found in the sputum. The x-ray findings are characteristic enough to suggest a diagnosis: uniform, rounded opacity which is not dense and is topped by a clear crescent. The clear crescent is always very thin. The dense mass is much larger than the surrounding clear space. The pulmonary cavity is surrounded by a thin line as in an air cyst; the lung is healthy up to the point of contact with the cavity and the fungus. The

shadows remain the same without increasing in size (for six years, case 2; five years, case 4). Atelectasis following bronchial obstruction was never observed. A patent lumen permitting the passage of air is always seen between the fungus and a dilated bronchus. The presence of fungus and its identification constitute the most convincing element in diagnosis. Repeated sputum examination should be carried out; the fresh mucopurulent particles should be examined microscopically after washing in physiological saline solution. A culture should be made; finally, innoculation into rabbits help the identification. In order to increase the chances of a successful culture, large portions of the mass must be removed aseptically from the surgical specimen and innoculated into at least 20 culture tubes. Certain authors recommend the trans-thoracic puncture. This method is not part of our usual practice. Skin testing with aspergillus may also be used.

Differential Diagnosis

Besides the search for tubercle bacilli, one can also resort to the Casoni test, to angiography, to search for cytological examination of the secretions aspirated by bronchoscopy and the use of serial x-ray films.

Certain x-ray pictures have a similarity with the picture of aspergilloma. Sequestrum can be produced by paraffinoma as well as by tumors of intrapulmonary angiomas, small hydatid cysts, filled cavities, and the typical picture in certain types not identified as tuberculous, and certain pendulous malignant or benign tumors. However these shadows do not show the extraordinary suggestive and permanent characteristics which we have described. These sequestra are not accompanied by the "sign of the tegmentum".

Treatment

Deep x-ray treatment, as applied by Dévé and Gerstl was without effect. Iodides, which did not seem to have any effect on our second patient, only promoted hemoptysis and produced iodism. Results were not more favorable with iodized oil instillation and besides, we know that iodide is ineffective in aspergillosis. This is also true for all the known antibiotics (Case 3).

Surgery remains the only treatment for aspergilloma, and we prefer segmental resection because of the simplicity and of the elective character of the operation.

Pathology

It is probable that the infection occurs through the respiratory tract. The question remains whether bronchial dilatation existed before the fungus infection or if previous bronchiectasis favored the localization of the fungus; the latter thus increasing the bronchiectasis.

A clean-cut answer cannot be given to either of these hypotheses. Hemoptyses of long standing are not a strong argument in favor of pre-existent bronchial lesion while the co-existence of bronchiectasis in other places

(cases 2 and 8) is to be noted. The frequency of saprophytic fungi in the respiratory tract is well known; the growth of fungi in a pathogenic state seems to call for special soil which might be furnished by bronchiectasis.

We believe it is as simple to admit that bronchial enlargement is secondary, that is aspergilloma is "bronchiectasis-producing". The location of the aspergilloma is always in an apex (seven cases, apex of the upper lobe, two cases apex of the lower lobe) while simple bronchiectasis is predominantly a disease of the lower portion of the lobes.

Several cases of aspergillosis are known to be *engrafted* on bronchiectasis. In such cases aspergillotic vegetation, with parietal infiltration is observed (Bryce and Podak).

Finally, there are other types of tumors which grow in bronchi and enlarge them: hydatid cyst or epithelioma. The epithelioma and other tumors obstruct the bronchus in which they grow and produce atelectasis and retrograde infection. On the contrary, a bronchus is never occluded by aspergilloma. A free space always exists around it where air circulates. It looks as if the bronchial wall was receding in front of the growing fungus.

The mycetoma is characterized by a heap of tangled filaments. These "grains" of mycetoma are forms of destruction and of resistance, which should explain the difficulty one finds in cultivating them and the absence of fructifications which would allow their exact diagnosis.

A precise identification of the mycelium involved could not be carried out in several of the above cases. In our last case, we were careful to make a complete mycological examination, including examination of the sputum, culture and inoculation of the "grain" and histological section. Everything seems to point to an Aspergillus Fumigatus as the agent. These examinations corroborate the incomplete observations of the previous cases and agree with the results of studies made by Dutch authors. Therefore we believe we are justified in replacing the generic term of megamycetoma by the more accurate term "Aspergilloma".

We were struck by the hemorrhagic character of the lesions. In the two cases where pneumotomy was performed, the operative hemorrhage was rather abundant and difficult to stop. Our second case had two serious hemorrhages during 48 hours following the operation.

By mere chance, a peculiarity was pointed out by Dévé after a section: he observed an artery, probably a branch of the pulmonary artery, which showed lesions of ectatic arteritis in a part of the cavitary wall. Its membrane of average elasticity was dissociated and ruptured at one point. An organized clot stretched from the artery to the enlarged bronchial cavity. Dévé believed that this arterial lesion was of enzymatic or toxic origin. Contrary to the arterial thrombosing lesions described by Macaigne and Nicaud in their cases of pulmonary aspergillosis, no penetrating of mycelious filaments in the vessels was observed.

SUMMARY

The characteristics of a new and rare disease, bronchial aspergilloma, have been defined using nine cases to illustrate the diagnostic points.

The pathological picture and the clinical aspects of this disease and its roentgenological characteristics have been described.

Aspergilloma is a pulmonary mycelium tumor due to the aspergillus, characterized by hemoptyses, absence of tubercle bacillus and a peculiar x-ray appearance.

Segmental resection appears to be the most satisfactory treatment for this disease.

We suggest that the name previously used "intrabronchiectatic megamycetoma Dévé" be discarded and that the lesion be known under the term of "bronchiectatis-producing".

RESUMEN

Se definen las caracteristicas de una enfermedad nueva y rara: el aspergiloma bronquial y se hace uso de nueve casos para ilustrar las caracteristicas diagnósticas.

Se describen tanto el aspecto clinico como el cuadro patológico de esta enfermedad y otro tanto se hace con el roentgenológico.

El aspergiloma es un tumor pulmonar miceliano caracterizado por hemoptisis, ausencia de bacilos de Koch y un aspecto peculiar a los rayos X.

Parece que la resección pulmonar es el tratamiento mas satisfactorio de esta enfermedad.

Sugerimos que el nombre antes dado de "megamicetoma intrabronquiectásico Dévé" se descarte y que la lesión se conozca bajo el termino de "bronquiectasógena" (bronquiectasis-producing).

RESUME

Les auteurs décrivent les caractères particuliers d'une maladie nouvelle et rare d'après 9 cas originaux. Ils lui ont donné le nom de "aspergillome bronchectasiant".

L'histoire clinique et les aspects radiologiques en sont caractéristiques.

L'aspergillome est une tumeur mycélienne constituée par l' "aspergillus". Elle est caractérisée par l'existence d'hémoptysies sans bacilles de Koch et par une image radiographique particulière.

La résection segmentaire semble être le meilleur traitement à lui appliquer.

Les auteurs suggèrent de transformer l'appellation de "mégamycétome bronchectasiant" proposé par Dévé en "aspergillome bronchectasiant".

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Bronchography*

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Intoduction

In 1922 Sicard and Forestier[1] advocated the introduction of iodized oil into the bronchial tree. Such contrast medium opacifies the bronchial lumen, rendering it possible to determine by radiography the lumen diameter of the bronchial tree. Bronchography has provided a means not previously available for the accurate diagnosis of many bronchial lesions and has unquestionably stimulated interest in the diagnosis of bronchopulmonary suppurative disease.

It has long been established that negative findings on conventional x-ray film studies do not exclude bronchial pathology. While bronchography is employed primarily for the diagnosis of bronchial pathology, it is on occasion helpful in the diagnosis of pulmonary parenchymal disease, such as pulmonary cavitation and abscess.

Accurate localization of the extent of bronchial disease is essential for proper surgical extirpation of the affected pulmonary segments. Preoperative demonstration of the extent of bronchopulmonary suppurative disease is a prerequisite to satisfactory surgical result. However, even with good bronchograms and accurate preoperative determination of the extent of disease, the surgeon may encounter difficulty in the operative localization and complete removal of the affected segments.

The aim in all bronchography for the diagnosis of bronchopulmonary suppurative disease is complete five-lobe filling. It is tragic that too often patients are referred to the hospital who have had incomplete and unsatisfactory bronchograms, showing inadequate mapping of all bronchopulmonary segments. Residual parenchymal iodized oil may persist for varying periods, obscuring lung detail to a degree that a repeat bronchogram, properly performed, is not immediately possible. This often results in a delay of weeks or longer in establishing a diagnosis and subsequent management.

In any form of lung disease, where the status of parenchymal lesions must be radiologically followed, it is best to avoid the use of iodized oil. The masking of the parenchymal lesion by the residual oil may last for weeks, and thus make serial film comparison difficult. This is especially true in tuberculosis. With the increasing use of good planigraphy and diagnostic bronchoscopy, there are but few indications for bronchography in tuberculosis, except when tuberculous bronchiectasis is felt to be the outstanding pathology.

Since the advent of examination of aspirated bronchial secretions by

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means of the Papanicolaou technique, bronchography for the demonstration of bronchial block due to bronchogenic carcinoma is seldom indicated.

In acute lung infections or in an acute exacerbation of a chronic lung infection, the use of contrast medium is contraindicated until the acute manifestations have subsided. Bronchiectasis frequently has exacerbations, when not only the patient's toxicity is greatly increased, but when increased parenchymal exudative phenomenon is radiologically demonstrable. Bronchography is best done after the subsidence of the exacerbation which can generally be controlled by the use of the indicated antibiotic.

There is no question that any case requiring a bronchogram should also have the benefit of bronchoscopy. While bronchoscopy has definite value in the diagnosis of bronchopulmonary suppurative disease, it has admitted limitations simply because it is impossible for the bronchoscopist to visualize the anatomical status of the bronchi except for a short distance beyond the main bronchi.

Various techniques used in bronchography have been reported by Carr,[2] Adams and Davenport,[3] Heublein and Gilfillan,[4] Jackson and Bonnier,[5] and Lynn.[6]

General Considerations

It is our conviction that the transnasal endobronchial catheter method is the ideal technique for bronchography, and we now employ this method exclusively.

Bronchoscopy is ordinarily performed several days before lipiodol bronchography. Antibiotic sensitivity tests are done on the bronchoscopically aspirated secretions. Preliminary to bronchography, several daily measurements of sputum are recorded. If the amount is more than 45 cc. in 24 hours, postural drainage is instituted and antibiotics are administered to decrease the amount of sputum. Penicillin or neo-penil have been the antibiotics most indicated in our experience.

Cocaine, 10 per cent solution, is our choice of topical anesthesia. While the amount of cocaine solution required to obtain satisfactory pharyngeal, laryngeal, tracheal and bronchial anesthesia may vary, we have found that 5 to 7 cc. are sufficient for the average adult case. Since 1936 we have had no alarming cocaine reactions. However, it is our regular policy to schedule all bronchograms with the Department of Anesthesiology so that, in event of a cocaine reaction, an anesthesiologist may be available for administration of oxygen, aspiration of secretions and artificial respiration. One fatality has occurred as the result of the use of pontocaine and we have discontinued employing this drug as an anesthetic.

For children, general anesthesia is necessary. Ether administered through an endotracheal tube is our anesthetic of choice, and the iodized oil is injected through a small catheter passed through the endotracheal tube.

Lipiodol, 40 per cent, is the iodized oil contrast medium which we have used in our series. Ordinarily we use lipiodol at room temperature. If the oil is warmed its viscosity is decreased and it flows too rapidly into pulmonary alveoli. In extremely hot weather the oil is kept in a refrigerator

until just prior to its use. Our main objective is to delineate all segmental bronchi without overfilling. The total amount of oil used in the average bilateral bronchogram is 30 cc. If bronchiectasis is saccular, extensive and bilateral, as much as 40 cc. of oil may be necessary for good bilateral bronchograms. In such cases the oil does not overfill the alveoli as it is quickly eliminated by coughing and by postural drainage instituted immediately following bronchography. It has been noted that the emphysematous areas in the parenchyma retain oil longer than other pulmonary or bronchial pathology.

A history of iodine-sensitivity is sought but no skin test is done, and we have encountered no cases of iodism in our series. Iodism is due mainly to the inadvertent swallowing, intestinal digestion and absorption of the iodized oil. With the transnasal endobronchial catheter method, however, the amount of oil swallowed by the patient is minimal. Our patients are instructed to expectorate rather than swallow any coughed-up secretion for a three-day period following bronchography. Theodos[7] reports a case of iodine sensitivity in a patient who was desensitized by administration of corticotropin both before and after bronchography.

We have found that the Stitz catheter is most satisfactory. Size No. 16 or 18 is optimal for adults. It is advisable to employ a smaller catheter for children.

Robertson and Forgan Morle[8] reported 16 delayed pulmonary complications in 220 consecutive bronchographies, five of which had pleural effusion. They noted that a delayed reaction never followed a repeat bronchogram, whether or not complications followed the first procedure. Our experience, using the transnasal endobronchial catheter method, is in contrast to that of Robertson and Forgan Morle. We have encountered no postbronchographic complications in our series of 503 cases.

Ideally, one lung only should be bronchographed at a single sitting, and an interval of three weeks should elapse before the other lung is mapped. In this period of time there will be sufficient clearing of the oil from the lung first bronchographed to obtain a clear, satisfactory and valuable lateral film of the contralateral lung at the second sitting. However, in the majority of instances, expediency dictates the necessity of establishing the status of the bronchi in both lungs at a single hospital visit. The desirability of prompt diagnosis and the economic factor of repeat or prolonged hospitalization frequently necessitate bilateral bronchography at a single sitting. When both lungs are to be mapped (the usual case) the more affected side is chosen first.

Technique

(Transnasal Endobronchial Catheter Method)

Bronchography is best performed in the morning, the entire procedure having been described to the patient on the previous day. This removes any doubt or fear, allays apprehension and insures better cooperation. We explain carefully that his complete cooperation is essential if a good result is to be obtained. As most patients will already have been bronchoscoped,

it is pointed out that bronchography is less rigorous, does not prevent head or body movements and does not involve any method of restraint. The patient is instructed to avoid ingesting food or liquid after midnight.

If the quantity of sputum has been 15 cc. or more in 24 hours, postural drainage is ordered on alternate 10 to 15 minute periods for two hours before bronchography. This drains the bronchi for better lipiodol filling and decreases the likelihood of coughing.

An hour before bronchography codeine sulfate, 30 to 60 mg., orally or hypodermically, and nembutal, 50 to 100 mg., orally, are given. These represent average adult dosages. When the patient arrives in the Department of Radiology, preliminary upright postero-anterior and lateral films are obtained to determine the optimum radiologic technique. Film exposure density approximately 8 KV. over proper conventional technique is desirable. One must be able to discern lipiodol shadows through shadows of heart, spine, etc. These films are inspected before proceeding with the bronchography. It is important that a technician well-versed in the procedures and radiography of bronchography be available. The importance of obtaining films in as short a time as possible following the bronchial instillation of oil cannot be overstressed. Dissipation of the oil into the alveoli can occur in a short time, and satisfactory bronchial mapping requires prompt radiography.

When the patient has been comfortably seated the nose, throat and larynx are examined and any abnormalities noted. The more patent nasal cavity is selected and a nasal speculum is introduced. With a cotton applicator cocaine (10 per cent solution) is applied to the inferior and middle turbinates and meati back to the posterior pharyngeal wall. The pharynx and anterior faucial pillars are sprayed with the same solution, the patient being instructed not to swallow but to expectorate into an emesis basin. The operator then holds the patient's tongue forward and, employing a curved laryngeal forceps holding a cotton pledget moistened with cocaine, anesthetizes both pyriform fossae. The larynx is now examined with a laryngeal mirror. With the patient holding his tongue forward, 0.25 cc. of cocaine are instilled into the larynx through a laryngeal cannula, the tip of which is just behind the epiglottis. Coughing usually results from this procedure.

The catheter is now passed through the inferior meatus. The patient holds his tongue forward and under guidance of the laryngeal mirror the catheter is introduced into the trachea. Cocaine, 0.25 cc., is injected into the catheter and the patient is requested to breathe deeply while tilted to the left; the procedure is repeated with the patient tilted to the right. This anesthetizes the tracheal and bronchial mucosa and suppresses the cough reflex. The patient is then placed in a standing position behind the upright fluoroscopic screen, and the position of the tip of the catheter is determined.

The position of the catheter is now adjusted until its tip has been passed just beyond the right upper lobe bronchial orifice; on the left side the tip of the catheter should be above or opposite the left upper lobe bronchial orifice. An adhesive strip is wrapped around the catheter and attached to

the skin of the cheeks to prevent catheter movement. If there is a tendency to cough, another 0.25 cc. of cocaine are injected through the catheter directly into the bronchus of the lung to be mapped. If coughing still persists, and the patient is unable to cooperate and suppress the cough reflex, the procedure is discontinued and the patient returned to his room. Further attempt may be undertaken the following day. We feel it is important to follow this rule rather than obtain an inadequate bronchogram.

Initially there is a tendency for the catheter to enter first the right

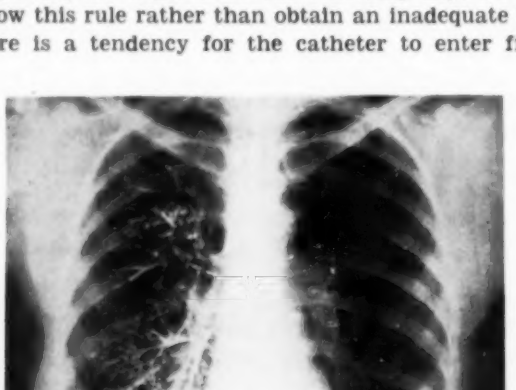
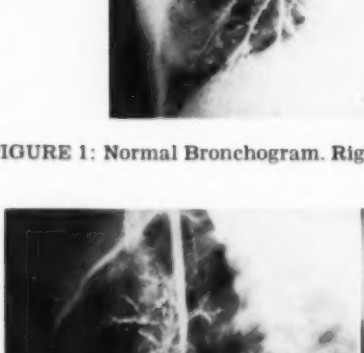


FIGURE 1: Normal Bronchogram. Right Lung. Postero-anterior projection.



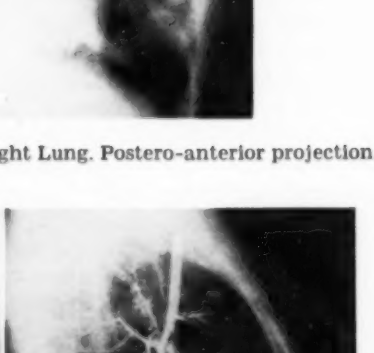


FIGURE 2 FIGURE 3

Figure 2: Normal Bronchogram. Right Lung. Left anterior oblique projection
Figure 3: Normal Bronchogram. Right lung. Right lateral projection.

main stem bronchus which is practically a continuation of the trachea. If there is difficulty in passing the catheter into the left main stem bronchus, this can be overcome by manipulation of the catheter and simultaneous rotation of the patient's head to the right. With the catheter placed in the proper position, depending upon which lung is to be mapped, we are now ready for the actual instillation of the oil. At this point we remind the patient that he must avoid coughing until the procedure is completed, but that he may clear his mouth and throat if necessary.

Right Lung Bronchography: At the beginning of oil instillation the tip of the catheter should lie just below the right upper lobe bronchial orifice. The patient is standing behind the fluoroscopic screen and a syringe containing 20 cc. of lipiodol has been attached to the catheter. No spillover will occur to the contralateral side since the catheter tip lies in the right main bronchus. The oil is slowly injected and, bending the patient first to the right and then to the left, the flow and distribution of this oil are observed fluoroscopically, until all basal segments are filled satisfactorily. No attempt is made to completely flood the bronchial lumen as more information is obtained by coating the bronchial wall with a thin, evenly distributed film of oil. After the basal segments are satisfactorily mapped, the patient is told to bend forward and to the right. Further oil is injected to map the right middle lobe bronchi. Having obtained sufficient injection of middle lobe bronchi, the fluoroscopic table and the patient are quickly leveled to a horizontal position, placing the patient in supine posture. Frequently there will be sufficient oil in the main stem bronchus to fill the superior segment bronchus of the lower lobe; if not, more is injected until fluoroscopic vision determines that this segment has been mapped. With the patient still in supine position, the catheter is slightly withdrawn until its tip lies at the level of the right upper lobe bronchial orifice. The patient's arms are then slowly extended above his head and at the same time he is rotated into a lateral position with his right side down. Additional oil is injected with fluoroscopic observation of its entrance into the anterior, apical and posterior segment bronchi of the upper lobe. It is usually necessary to rotate the patient into oblique and, at times, prone positions in order to obtain complete mapping of all segments of the upper lobe. In order to obtain sufficient filling of the apical segment bronchi to their termination, it is usually necessary to tilt the fluoroscopic table to a Trendelenburg position and request the patient to take several deep breaths.

During the entire procedure of the bronchography constant check of the flow and distribution of oil is obtained by intermittent fluoroscopic observations. Spot or flash films are obtained during this fluoroscopic procedure, as deemed necessary for the demonstration of abnormalities of bronchial lumen. When all bronchi of the right lung have been satisfactorily visualized the patient is immediately returned to standing position, and films are immediately taken in the following order: right lateral, left anterior oblique and postero-anterior projections. We employ a 48-inch film target distance. It has not been our experience that in bronchography stereoscopic projections offer any significant values.

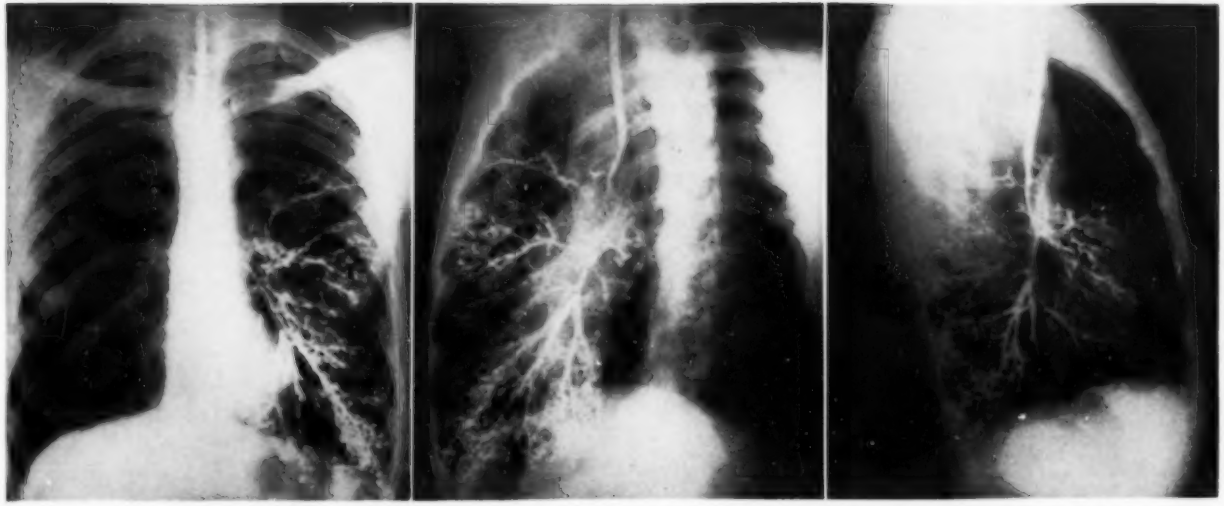


FIGURE 4 FIGURE 5 FIGURE 6

Figure 4: Normal Bronchogram. Left Lung. Postero-anterior projection.
Figure 5: Normal Bronchogram. Left Lung. Right anterior oblique projection.
Figure 6: Normal Bronchogram. Left Lung. Left lateral projection.

Left Lung Bronchography: The procedure for left lung bronchography is nearly identical with that for the right lung. The catheter is passed and manipulated into a position just above the left upper lobe bronchial orifice. The initial bronchial instillation of the oil is made with the patient standing. The filling of the basal segments of the left lower lobe is identical to the procedure for the right side. Following this the patient bends forward and to the left, and further oil is injected to fill the bronchi of the lingula. The remainder of the procedure is exactly the same as for the right lung, except that the tip of the catheter is placed at the level of the left upper lobe bronchial orifice for complete mapping of the upper lobe segments. Films are obtained in the following order: left lateral, right anterior oblique and postero-anterior projections.

Bilateral Bronchography: If both lungs are bronchographed at the same sitting, the lateral projection is deleted for the second lung. A lateral film of the second lung is almost valueless due to confusing lipiodol shadows in the first lung.

The most valuable films in any bronchogram are the lateral and the oblique projections.

Figures 1-6 show normal and complete filling of the various segmental bronchi of both lungs.

SUMMARY

The aim in all bronchography for the diagnosis of bronchopulmonary suppurative disease is complete five-lobe bronchial mapping. Accurate localization of the extent of bronchial disease is essential for proper surgical extirpation of the affected bronchopulmonary segments. It is deplorable that good bronchography is the exception rather than the rule.

It is the authors' opinion and firm conviction that the transnasal endobronchial catheter method is the ideal technique for bronchography. Preliminary sedation (codeine and nembutal) is advisable. Cocaine is the topical anesthetic of choice. Lipiodol is the contrast medium preferred and the Stitz catheter is satisfactory.

Ideally only one lung should be bronchographed at a single sitting; however, expediency often dictates the necessity of establishing the status of the bronchi of both lungs at a single hospital visit.

A detailed description of the technique of the transnasal endobronchial catheter method is given. No post-bronchographic complications have occurred in a series of 503 cases.

RESUMEN

El objeto de toda broncografía diagnóstica de supuraciones bronchopulmonares, es la visualización de los bronquios de los cinco lóbulos. Es esencial la exacta localización y extensión de la enfermedad bronquial para la adecuada extirpación quirúrgica de los segmentos afectados. Es de deplorarse que la buena broncografía, es más de excepción que la regla.

Es opinión de los autores, así como su firme convicción, que el método transnasal endobronquial, es la técnica ideal para la broncografía. Es de

aconsejarse, la sedación previa por el nembutal y la codeina. La cocaina, es el anestésico local de elección. El lipiodol, es el medio de contraste preferido y el cateter de Stitz, es satisfactorio.

Idealmente, sólo un lado debe broncografiarse en una sesión, pero a menudo, es más expedito, es necesario establecer las condiciones de ambos lados de una vez.

Se da una detallada descripción de la técnica para la instilación intranasal endobronquial. No ha habido complicaciones post-broncográficas en 503 casos.

RESUME

Le but de toute bronchographie dans le diagnostic des suppurations bronchopulmonaires est d'établir une topographie bronchique complète des cinq lobes. Une localisation précise de l'extension de l'affection bronchique est capitale pour assurer l'extirpation chirurgicale convenable des segments bronchopulmonaires atteints. Il est à déplorer qu'une bonne bronchographie soit l'exception plutôt que la règle.

Les auteurs ont la ferme conviction que l'introduction transnasale de la sonde endobronchique est la technique idéale pour la bronchographie. Une première action anesthesique peut être demandée à la codéine et au nembutal. La cocaine est l'anesthésique local de choix. Le lipiodol est le meilleur milieu de contraste et la sond de Stitz donne des résultats satisfaisants.

Il serait préférable de pratiquer la bronchographie pour un poumon seulement par séance. Cependant, les circonstances amènent souvent à établir l'état des bronches des deux côtés lors de l'unique visite à l'hôpital.

Les auteurs font une description détaillée de la technique de la sonde endobronchique par voie transnasale. Sur une série de 503 cas, il n'y eut aucune complication post-bronchographique.

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Mechanisms of Fatal Pulmonary Hemorrhage in Tuberculosis

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Fatal hemorrhage is not an uncommon mode of exitus in patients afflicted with pulmonary tuberculosis. Perhaps the most disturbing feature is that many of the individuals who are stricken have passed the acute phase of their illness and apparently are on the road to recovery.

The incidence of fatal hemorrhage has been estimated by different authors to be from 1 to 5 per cent.[1] A survey of 2,500 autopsies at the Municipal Tuberculosis Sanitarium revealed that 109 cases (4.36 per cent) died in this manner. Of this total, 70 were men and 39 were women, and the greatest incidence was in the age group 20 to 29 years (Figure 1). The youngest and oldest individuals to suffer fatal hemorrhage were 11 and 65 years of age respectively. Of the 109 only 49 gave a history of having had any previous bleeding or hemorrhage. The chronicity of the disease was certainly a factor, the interval of time varying from one month to 21 years, and 33 patients gave a history of having had the disease for a period of four years or over. Twenty-two had pneumothorax for varying lengths of time, the maximum being four years, however, their disease was of such a nature that in only a few instances was any beneficial effect noted clinically, and no relationship to hemorrhage could be shown. The most common complication was amyloidosis—24 cases (22 per cent), showed gross and/or microscopic evidence of amyloid degeneration (this is about the same percentage as is seen routinely in our autopsy work). There was one case each of hypertensive heart disease, chronic glomerulonephritis, syphilis, and silicosis.

There is no chronological pattern as to the occurrences of these fatal hemorrhages. For example, in the years 1933, 1934 and 1935 several were recorded, and the next comparable number was in the middle 1940's; however, the highest total for any single year occurred in 1949. In spite of the chemotherapeutic and surgical measures employed in the past few years the incidence of fatal hemorrhage has remained about the same. Since chronicity is a fact it stands to reason that procedures which prolong the course of the disease also increase the likelihood of sudden fatal hemorrhage. This is especially true in cases which are far-advanced at the time of admission to the sanitarium. (During the last five years this group comprised 75 per cent of all admissions to our institution.) One cannot discount the observations of Petersen[2] in which he correlated hemorrhagic episodes in the tuberculous patient with conditional changes in the meteorological environment. These episodes he associated with blood pressure increases attributable to pressor changes.

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One usually associates fatal pulmonary hemorrhage with the rupture of an artery adjacent to or a part of a parenchymal cavity wall following an aneurysmal dilatation. These dilatations have been termed Rasmussen's aneurysms as Doctor Vald Rasmussen was the first to describe them in 1868.[3] The number of these lesions identified in different institutions varies greatly and perhaps to some extent in proportion to the time spent dissecting the specimens. Proliferative and reparative processes usually prevent aneurysmal formation within tuberculous cavities by occluding the blood vessels before their walls are destroyed. Because of the magnitude of the hemorrhage and the destructive and/or reparative processes going on in the lung, it is almost impossible to demonstrate the site of bleeding; this is especially true in those cases in which the bleeding apparently results from the rupture of an aneurysm; whereas bronchial lesions which perforate or erode the adjoining vessel can be demonstrated with relative ease. Rasmussen pointed out in his article that many men before him had attempted to explain the causes and mechanisms of fatal pulmonary hemorrhage but had been rather unsuccessful in their attempts. Laennec supported the idea that frequently pulmonary hemorrhage came about by a diapedesis of blood through the bronchial mucus membranes. A factor favoring this theory was that vessels in the vicinity of the cavity, especially in the fibrous wall, were usually obliterated. This was true also for vessels which traversed the cavity, however, we know now that many of these vessels remain open. Andral was of the opinion that there were three possible sources of pulmonary hemorrhage: first, that seen in conjunction with a tuberculous endobronchitis, however, he was not in a position to demonstrate the actual bleeding point; second, bleeding in cases of pulmonary apoplexy (it is assumed that by this he meant vascular disturbances such

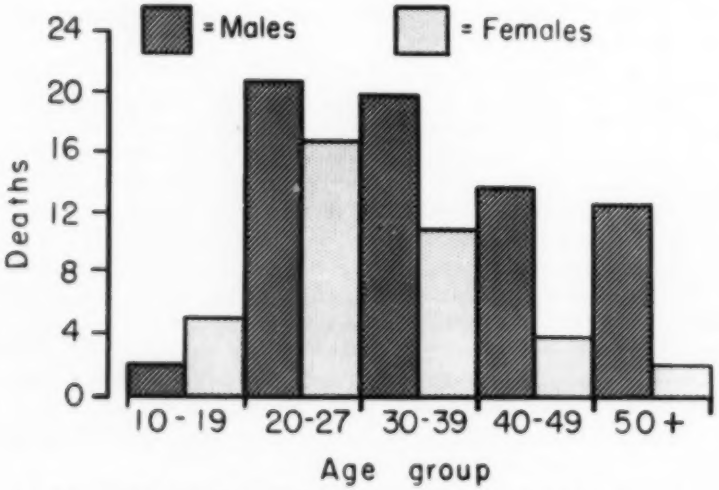

FIGURE 1: Graph depicting the incidence of fatal pulmonary hemorrhage according to age and sex.

as hemorrhagic infarctions) and third, hemorrhage from a cavity. In this instance Andral was able to demonstrate a bleeding vessel in only one case—a vessel that was enclosed in a trabeculum crossing the cavity. Rokitansky was about the only writer who had described cases such as simulated those of Rasmussen. According to Rokitansky the copious hemorrhages seen in tuberculosis easily arose from branches of the pulmonary arteries situated in the condensed walls of cavities, especially bronchiectatic cavities. He was of the opinion that the vessel walls became macerated, jelly-like and soft due to exposure to the contents of the cavity and necrotic processes in the wall of the cavity so that finally they would burst into the cavity and a massive hemorrhage would take place. The lesion he described as either a split-like fissure in the vessel or the separation of a portion of the vascular wall gave rise to a punched-out defect. Very frequently this punched-out defect was seen in an aneurysmal dilatation of the vessel towards the cavity.

Rasmussen's observations were based on the examination of 11 cases who died during a violent hemoptysis. Eight of these were patients in whom there was a rupture of a vessel running in the wall of the cavity and the other three were instances of rupture of an aneurysm of the aorta into the bronchus or into the pulmonary tissue itself. Of the eight cases in which hemorrhage was due to a rupture of a vessel adjacent to a cavity, four demonstrated rupture of a small sac-like aneurysm which had developed on a branch of a pulmonary artery running in the wall of the cavity, and four showed dilatation or ectasia of a branch of the pulmonary artery with operculated rupture. These aneurysms varied in size from that of a pea to a walnut. The wall varied in thickness and in those which had not ruptured the wall was seen to be two or three times thicker than the rest of the vessel. The lesions were sometimes multiple and the vessels on which the aneurysms were located averaged from one to three millimeters in diameter.

Plessinger and Jolly[4] studied a series of 667 cases from the years 1938 to 1947 and of these 49 died of massive pulmonary hemorrhage. In 29 of these cases they were able to demonstrate an aneurysmal dilatation of a vessel. On the basis of their histological studies, they describe the incriminative vessel as usually running tangential to the wall of the cavity. As the vessel broached the wall of the cavity it passed through its own diseased pulmonary tissue and started to dilate slightly. Concomitantly a variable degree of endothelial thickening usually occurred so that the lumen of the vessel was slightly constricted. Similar obliterative endothelial changes were observed in the other large vessels in the vicinity of the cavity wall. Serial sections revealed that the vessel wall proper dilated eccentrically; the dilatation taking place only on the side toward the lumen of the cavity. Finally a point of rupture of the media was encountered. A great deal of emphasis is placed on the presence of a fibrin clot in every unruptured aneurysm and in some of the ruptured aneurysms. They are in agreement with Rasmussen's theory that this clot may occasionally plug the rent in the aneurysmal sac and thus prevent a fatal hemorrhage for some time.

O'Leary[5] reported a death occurring in a nine month old infant in which instance a recently ulcerated cavity eroded a large vessel. Certainly some of the cavities seen appear to be so rapidly excavating that proliferative changes in the neighboring blood vessels do not take place.

Codina Suque and Mansilla Delicado[6] felt that bleeding might be the result of a profuse diapedesis of blood into the alveolar spaces quite removed from an active tuberculous process, or at least from an ulcerating lesion. They were of the opinion that what was commonly considered to be post-hemorrhagic "seeding" probably represented hemorrhagic areas complicating preexisting tuberculous foci. The preexisting tuberculous involvement we would assume to have been a recent bronchogenic or hematogenous dissemination from a "spilling" lesion elsewhere in the parenchyma or lymph nodes. These workers emphasize that it is not necessarily the amount of blood lost but the impingment on functional lung parenchyma which accounts for death.

Quiroga[7] points out that fatal hemorrhage may be the result of a rapidly ulcerating caseous pneumonia (necrotic pneumonia of Sabourin) or from a rupture of small vessels constituting the vascular make-up of cavity walls. However, we have not seen sufficient evidence of bleeding from granulation tissue such as lines most tuberculous cavities to account for a fatal hemorrhage in any of the cases studied. Kiosk[8] reported a case of fatal hemorrhage due to rupture of a large branch of the pulmonary artery without aneurysmal formation—a circumstance he considered unique.

The inconsistency of the mechanism of fatal hemorrhage can best be illustrated by the following case reports:

Case 1: H.G., a 23 year old white man born in Chicago, contracted a severe cold with pleurisy and about 10 months later pulmonary tuberculosis was diagnosed. Pneumothorax was instituted and abandoned after a few treatments. He had

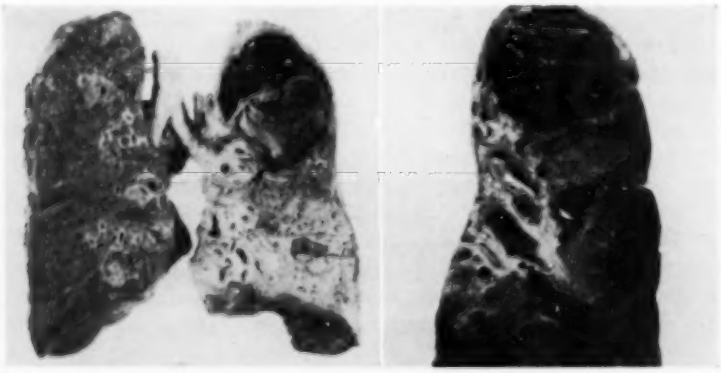

FIGURE 2 FIGURE 3

Figure 2: Sagittal sections through the lungs showing two aneurysms filled with laminated blood clots and a huge cavity in the left apex filled with recently clotted blood.—*Figure 3:* A Section through the left lung showing a large cavity in the apex filled with clotted blood and a small cavity in the mid-portion with a probe extending from the branch of the right pulmonary artery into the cavity.

frequent small hemorrhages and succumbed to a massive hemorrhage approximately 18 months after the onset of illness.

Pathology: There was considerable involvement of the left lung, as seen in Figure 2, and in the lower portion of the upper lobe cavity a huge laminated blood clot was found, and a small circular cavity in the lower lobe also contained a laminated blood clot. Infiltrations were noted in the opposite lung and there was considerable involvement of the pleura covering the organ. Here, we are dealing with two aneurysmal dilatations both filled with clotted blood and a rent in the wall of the larger one was responsible for a massive hemorrhage.

Case 2: M.J., a 35 year old foreign-born white woman whose husband had died from pulmonary tuberculosis one year before her admission. Her health was good, she maintained, until one month before coming to the sanitarium. Physical examination was essentially normal except for the chest which revealed dullness to percussion over the left lung and harsh breath sounds over both apices. X-ray film inspection revealed considerable involvement of the left lung and the sputum was positive for acid-fast bacilli. Her course was progressively downhill and she died six months after admission to the sanitarium with laryngeal and intestinal complications. Death, however, was sudden with a massive pulmonary hemorrhage.

Pathology: Examination of this lung (Figure 3) revealed a 7 cm. cavity in the apex which was filled with a dark red blood clot. There was a smaller cavity measuring 2.5 cm. in diameter in the upper part of the lower lobe which was filled with what appeared to be an older clot and into this cavity protruded a 1.5 cm. aneurysmal dilatation of the pulmonary artery. Careful dissection revealed a rent in the wall of this aneurysmal dilatation which was the source of the bleeding.

Case 3: A.P., a 35 year old Negro woman entered the sanitarium approximately six months after the onset of illness. She had been coughing and expectorating considerable material prior to admission and there was occasional blood streaked sputum. She was known to have had hypertension for some time and her blood pressure on admission was 195/120. Previously induced pneumothorax on the right obscured the physical findings but x-ray film revealed considerable disease in the right lung with most involvement apparently in the mid-lung field. In spite of supportive therapy her disease progressed and was complicated by severe tuberculous laryngitis. Approximately 16 months after admission to the sanitarium she expired suddenly with massive pulmonary hemorrhage.

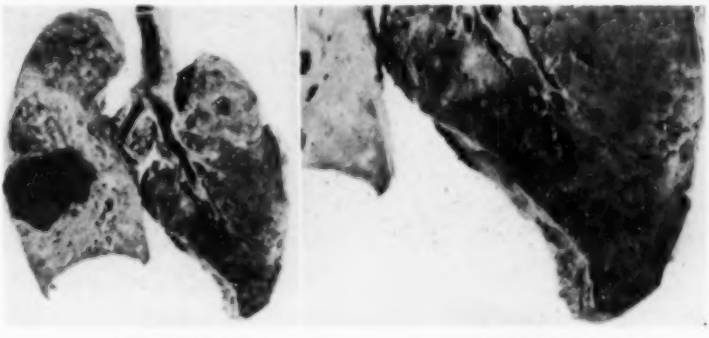

FIGURE 4 FIGURE 5

Figure 4: Sagittal sections of the lungs showing a large cavity in the left lower lobe filled with dark red clotted blood and scattered collections of blood throughout the opposite lung along with a large clot in the right main bronchus.—*Figure 5:* Close-up of the right lower lobe to show the flooding of the acini with blood.

Pathology: A middle section of the lungs (Figure 4) showed a large cavity in the left lower lobe with a heavy fibrous wall surrounding it and pneumonic consolidation in the adjacent parenchyma. The remainder of the lungs showed a flooding of the acini with blood (Figure 5). No residue of an earlier infection could be found and because of the nature of this lesion it was considered a young adult primary infection. Dissection failed to reveal any aneurysmal dilatation of a vessel; the source of hemorrhage was apparently the erosion of a branch of the pulmonary artery.

Case 4: W.N., a 43 year old white man whose mother had died from pulmonary tuberculosis when he was seven years of age. He was in fairly good health until four years before admission, at which time he had a severe cold with a cough and pulmonary tuberculosis was diagnosed. He had been in and out of the sanitarium on numerous occasions, usually leaving against medical advice. Six months before final admission he suffered severe pulmonary hemorrhage and continued to have blood-streaked sputum afterwards. He was a known alcoholic and physical examination revealed a poorly nourished white male who showed evidence of marked weight loss (50 pounds) with physical findings of a markedly enlarged liver, dullness over the right lung field and many rales over the entire right lung and the mid-portion of the left lung. During his six months stay in the sanitarium his lung picture did not change significantly but he had marked albuminuria, positive congo red test for amyloidosis, evidence of liver malfunction and sputum positive for acid-fast bacilli. He had a sudden massive pulmonary hemorrhage and expired.

Pathology: There was a huge dark red blood clot projecting out of the larynx (Figure 6) and on sectioning the lungs one saw that there was cavitation in both upper portions, that on the right being more extensive and most of the cavities were filled with dark red clotted blood. Extensive disection failed to reveal the point of rupture of the pulmonary artery. The cyst-like cavities in the upper portion of the right lung communicated with bronchi and apparently represented old tuberculous cavities which had re-epithelialized (Figure 7).

FIGURE 6

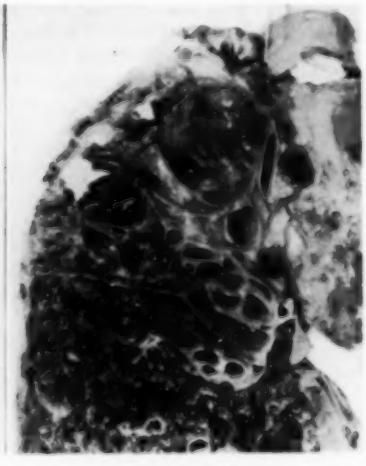

FIGURE 7

Figure 6: Close-up of the larynx and upper portion of the trachea with a huge blood clot in place as was found at the time of post mortem examination.—*Figure 7:* Close-up of the anterior portion of the right apex showing the epithelialized cavities and revealing the smooth glistening nature of the lining with the exception of a portion of the cavity laterally situated which showed considerable ulceration and may have been the source of bleeding.

Case 5: S.F., a 43 year old Negro man who was born in Memphis, Tennessee, and had worked as a sand blaster for 14 years. The onset of his illness was approximately one year before admission to the sanitarium. His chief complaint was weakness; there had been one episode of hemoptysis. Approximately two weeks after entering the sanitarium he suffered a massive fatal hemorrhage.

Pathology: Sagittal sections revealed a large cavity in the right lung surrounded by consolidated parenchyma (Figure 8). Small firm nodulations were felt in portions of the lung. The left lung showed a cavity in the mid-portion and there were several caseous infiltrates noted in the lung parenchyma, especially in the upper portion. Smaller ulcero-caseous lesions were noted throughout the right lung.

FIGURE 8

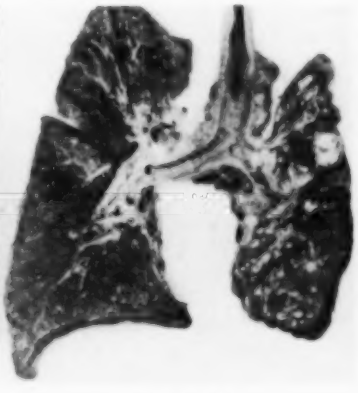

FIGURE 9

Figure 8: Sagittal section through the lungs showing bilateral cavitation and the huge blood clot in the trachea and main stem bronchi. The hilar lymph nodes were markedly enlarged and showed caseous infiltrations. The peribronchial nodes on the left showed calcified lesions.—*Figure 9:* Sagittal section of the lungs demonstrating ulceration of the right main bronchus and its secondary branches and multiple fibrocaseous lesions in the parenchyma of the right lung.

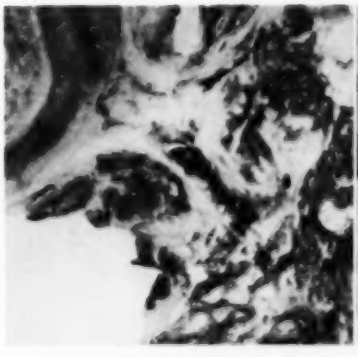

FIGURE 10

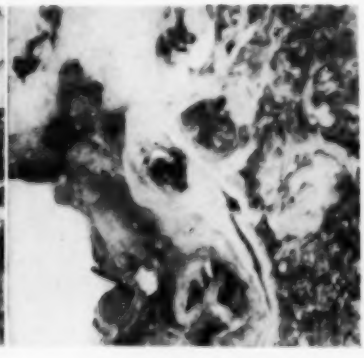

FIGURE 11

Figure 10: Close-up to illustrate the ulceration of the right main bronchus showing the clot in place and the eliptical defect superior to it.—*Figure 11:* The reverse side of the lung showing the defect in the right pulmonary artery through which the blood escaped into the bronchial tree.

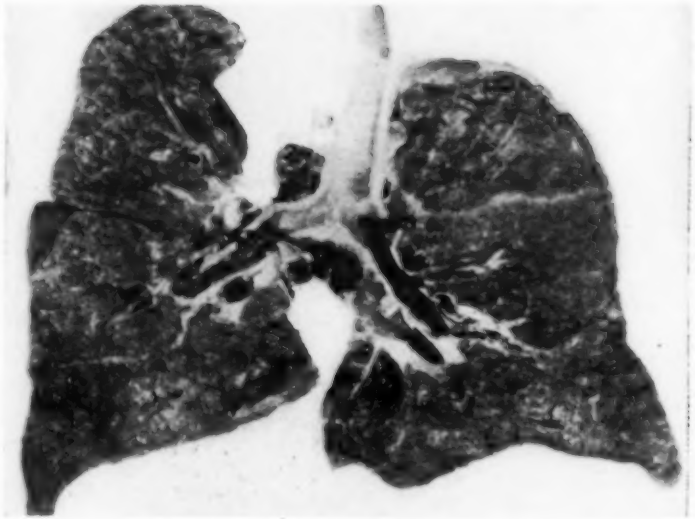

FIGURE 12

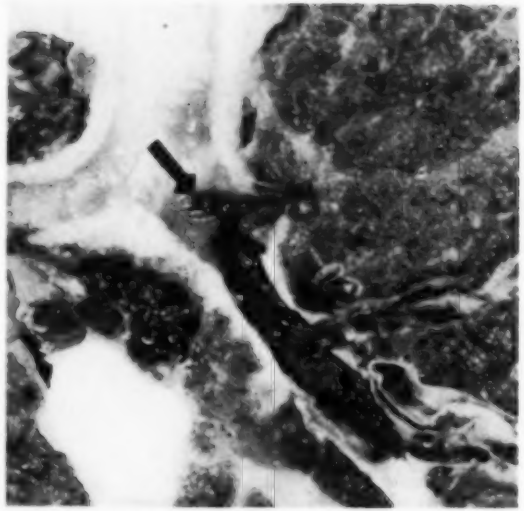

FIGURE 13

Figure 12: Sagittal section through the lungs showing both major bronchi and secondary bronchi filled with dark red clotted blood and darkly pigmented lymph nodes.—*Figure 13:* Close-up to show the black peribronchial node projecting through the anterior wall of the right main bronchus.

The lymph nodes were hard and rubbery in consistency and on section showed whirls of fibrous tissue indicative of some degree of silicosis. None of the cavities showed a definite limiting fibrous wall and careful dissection failed to reveal a bleeding point. This undoubtedly represents a case of erosion of a vessel wall by one of these rapidly ulcerating lesions.

Case 6: T.I., a 61 year old white foreign-born woman who was known to have pulmonary tuberculosis for at least nine years before admission to the sanitarium. During that time she had three or four acute febrile episodes but at no time did she require sanitarium care. Her husband had died from tuberculosis about six years before and x-ray films were taken periodically to determine the status of her pulmonary lesion. A febrile episode two months before admission was accompanied by high temperature, pain in the chest, cough, fatigue, and weight loss, and she expectorated a few cc. of yellowish sputum which was positive for acid-fast bacilli. Sanitarium care was recommended. Aside from a blood pressure of 170/100 physical findings upon admission were limited chiefly to the right lung which revealed slight dullness on percussion and limited excursions. No rales were heard in the chest at the time of admission. During her stay in the sanitarium she was given a course of streptomycin for approximately 90 days with some improvement. Bronchoscopy revealed a tuberculous endobronchitis on the right with bronchostenosis. Because of this finding, right pneumonectomy was considered but she refused surgery. She was ambulatory for the most part during her stay in the sanitarium and occasionally showed some blood streaking of the sputum. Approximately 18 months after admission to the sanitarium she experienced a massive pulmonary hemorrhage.

Pathology: A mid-section of the lung showed several fibrocaseous infiltrations scattered throughout the right lung with some fibrosis and retraction of the right apex (Figure 9). A rather large solitary fibrocaseous lesion was noted at the periphery of the right mid-lung field. There was marked ulceration of the mucosa of the mainstem bronchus and the secondary bronchi on the right. In the anterior portion of the lower lobe bronchus, a few centimeters from its origin, a large oval defect was noted (Figure 10); this defect was almost entirely filled by an organized blood clot, however, there was a small eliptical opening superior to the clot through which a probe could be passed to communicate with the adjacent pulmonary artery. This case demonstrates well the erosion of a main vessel (Figure 11) by a long standing tuberculous endobronchitis.

Case 7: M.P., a 61 year old white woman, foreign born, gave a history of having had the "flu" several times. For one year prior to admission she had slow progressive loss of weight and a few days before suffered a rather severe hemoptysis with streaking of the sputum every day thereafter. She entered a private hospital where a diagnosis of tuberculosis was made. Her sputum was positive for acid-fast bacilli and other laboratory examinations were negative with the exception of low grade hypochromic anemia. On bed rest over a period of six months she gradually improved but suddenly expired with a massive pulmonary hemorrhage.

Pathology: At autopsy a defect was found in the left upper lobe bronchus. This defect measured 6 mm. in diameter and the base of it was formed by a firm peribronchial lymph node (Figures 12 and 13). In the right main bronchus the mucosa was extremely thin and transparent and pigmented peribronchial nodes could be seen shining through. The hemorrhage arose from the bronchial artery which was eroded by the hard tuberculous node.

Case 8: H.Z., a 26 year old white man was visiting friends in the city when he suffered a pulmonary hemorrhage and was admitted to the sanitarium as an emergency. He had never been treated in a tuberculosis sanitarium but he stated that at the age of two years he had whooping cough which necessitated hospitalization for 24 months. Subsequently, when he was admitted to grammar school

FIGURE 14

FIGURE 15

Figure 14: Sagittal section of the lung showing the small, round necrotic area in the right bronchus at the mouth of the right upper lobe branch. Only small fibrocaseous foci are apparent. No evidence of cavitation was found. — *Figure 15:* Close-up showing the necrotic lesion and the slightly enlarged hilar lymph node. The node contains some small caseous infiltrations.

a chest x-ray film was taken and his parents were informed that there was considerable scarring of his lungs compatible with healed tuberculosis. In the years following he was hospitalized frequently because of his "weakened" condition. He stated that recently he had developed slight cough with a very small amount of expectoration, experienced some chest pain, and had mild dyspnea on exertion. Occasionally there were evening temperature elevations up to 101 degrees F.

Physical examination revealed a well developed and well nourished white man apprehensive and acutely ill. Examination of the chest showed impaired resonance and bronchial breathing over the right base. Sputum specimen was negative for acid-fast bacilli. Three days after admission to the sanitarium he suffered a severe pulmonary hemorrhage and expired.

Pathology: A mid-section of the lung disclosed a few small fibrocaseous tubercles in the upper portion of each lung. These tubercles appeared to be fairly well encapsulated. At a point in the right bronchus where the upper lobe bronchus takes its origin there was a necrotic area approximately 1.0 cm. in diameter (Figures 14 and 15) and a section of this lesion revealed that the entire bronchial wall was involved in this necrotizing process. This lesion eroded a branch of the bronchial artery and was responsible for the massive hemorrhage that was seen. The parenchymal disease was quiescent.

Discussion

Probably a massive hemorrhage produces death by suffocation, although in some instances, the loss of blood itself may be sufficient to terminate a cachectic individual. An estimation of the actual blood loss is difficult, as one must consider the amount of blood coughed up and expelled and that found in the lung and gastro-intestinal tract at the time of post-mortem examination. There is not much doubt that, in some cases, the total volume approximates 1,000 cc. Most patients die suddenly following a massive hemorrhage, and do not present the picture of exsanguination. The amount of blood necessary to produce death by suffocation probably varies greatly and is dependent upon several factors. When the main airways are filled to overflowing (as seen in Figures 7 and 8) undoubtedly the individual is asphyxiated by his own blood. On the other hand, collections of blood in the functional parenchyma in a lung partially destroyed by a previous disease (as seen in Figure 5), and with limited reserve may likewise asphyxiate an individual even though the volume of blood is not so great.

The presence of a definite aneurysm has been the exception instead of the rule in the routine examination of lungs from fatal hemorrhage cases at this institution. It was impossible to identify the bleeding vessel in many cases, however, this is true in instances of hemorrhage from other organ systems. A compilation of the findings in 50 consecutive cases is listed below:

Bleeding Point	*No. of Cases*	
None identified	36	
Pulmonary artery (no aneurysm)	8	
Rasmussen aneurysm	4	
Bronchial artery	2	
TOTAL		50

Even though the caliber of the involved vessels varied considerably in different cases no correlation could be made between the size of the vessel and the magnitude of the hemorrhage or the rapidity of death. Profuse

hemorrhage from the small bronchial arteries correspond to hemorrhages from the larger pulmonary artery branches because of the differences in pressure. The pressure in the lesser (pulmonary) circulation is estimated to be about one-sixth (mean value) that of the greater (systemic) circulation. Since the bronchial artery is derived from the aorta the pressure, no doubt, is consistent with systemic pressure. When the lung has wide spread involvement, the amount of blood flowing through the pulmonary arteries to the affected parts is proportionately reduced and the pressure is correspondingly less. Recent work by Marchand et al.[9] has shown that the pattern of the bronchial arteries varies considerably in disease, however, the pressure within the vessels probably is not altered to any appreciable degree. In the two instances (Cases 7 and 8) where the bronchial artery was the source of bleeding, the lesion was located near the main trunk of the vessels. Whether the smaller ramifications of the vessel are ever involved is questionable; it is our feeling that a branch of the pulmonary artery is the most likely source of hemorrhage at any point in the lung distal to the secondary bronchi.

The cases presented emphasize the multiplicity of mechanisms involved in fatal massive hemorrhage. It is true that many cases show a ruptured Rasmussen's aneurysm (and the incidence of this lesion varies with different institutions) but the majority reveal only an erosion of a branch of the pulmonary artery without any significant aneurysmal dilatation.

SUMMARY

A survey of 2,500 autopsies at Municipal Tuberculosis Sanitarium, Chicago, was made and a report of 109 cases whose deaths were attributable to pulmonary hemorrhage were analyzed. Selective cases were described in detail to illustrate the different mechanisms of massive hemorrhage and a review of the literature given.

RESUMEN

Se hizo una revisión de 2,500 autopsias en el Sanatorio Municipal de Chicago, entre ellas 109 muertes, fueron atribuidas a la hemorragia pulmonar. Se describen casos seleccionados en detalle para ilustrar los mecanismos diferentes de la hemorragia voluminosa y se revist la literatura al respecto.

RESUME

L'auteur à fait l'étude de 2,500 autopsies au Sanatorium Municipal de Chicago, et rapporte 109 cas dont la mort est imputable à une hémorragie pulmonaire. Il retient des cas significatifs pour illustrer les différents mécanismes de l'hémorragie massive, et fait la revue de ce qui à été publié sur ce sujet.

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Hemophilus Influenzae Bacillus in Viral Pneumonias

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During an epidemic of primary atypical (viral) pneumonia observed over a two month period, it was noted that Hemophilus influenzae bacillus was found as a complicating factor in 22 per cent of the cases. In this two month period, 186 patients with atypical pneumonia were admitted to the hospital. In 41 (22 per cent) moderate to abundant growth of H. influenzae bacillus was found by culture of material from the sputa and pharynx. Some of the patients having these organisms had a more severe illness than others with pneumonitis but who had normal bacterial flora. For this reason a comparative study has been made of 300 consecutive cases of pneumonitis in an attempt to determine whether H. influenzae bacillus as a secondary invader may adversely affect the course of virus pneumonia. This study is divided into two groups and will be referred to as the Hemophilus influenzae bacillus group, and the control group. There are 41 cases in the H. influenzae group and 259 in the control group.

The role of H. influenzae bacillus in pneumonias has been considered to be one of probable secondary invasion, acting possibly in symbiosis with certain viruses.[1] Reimann[2] states that the influenza bacillus, unaccompanied by other bacteria, is not a common cause of pneumonia. Its incidence in pneumonia varies from year to year. By itself, it probably causes less than 2 per cent of all cases of pneumonia. Even then, there is often an uncertainty as to the presence of a virus infection as a causative agent. The pneumonia caused by the Hemophilus bacillus usually arises as a secondary infection in sporadic cases where the resistance of the body is lessened by other causes, chiefly by infections of the respiratory tract. Dingle et al.,[3] found by the use of selective medium that Hemophilus species occurred in 80 to 100 per cent of all cases in all groups (of respiratory diseases) at some time during the course of illness. From these studies they concluded that the bacteria present, including H. influenzae bacillus, were essentially those considered normal for the respiratory tract.

In Hawaii, there appears to be an endemic occurrence of pneumonitis having most of the characteristics associated with a viral etiology and which has no relation to age, sex, or season of the year. This condition was brought to the attention of the medical profession by Bowen in 1935.[3] Reports of

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a pneumonitis in young adult males in the United States were made by Gallagher[4] and Allen[5] at about the same time. Subsequent to these early reports there have been many interesting studies reported of pneumonias of probable viral origin.[6-8] The criteria used for diagnosis in all cases consisted primarily of demonstrating pneumonitis by x-ray film of the chest in patients complaining of acute respiratory infection. Virus studies were not made because of a lack of facilities. Previous experience with this type of pneumonitis in military personnel has been such that cold agglutinins were demonstrated infrequently, which is not in accord with other reports.[13] In both groups cold agglutinins were demonstrated in less than 10 per cent of those tested. Three hundred consecutive cases of pneumonitis seen in an 11 month period are reviewed and comparisons made with those demonstrating H. influenzae bacilli. These patients were either military personnel or their dependents. There was no death in this series. One hundred and four of the first 200 cases came from newly inducted Army recruits who had recently arrived from continental United States. The last 100 consecutive cases of pneumonitis observed showed only 13 occurring in a similar group of recruits.

Of the 41 cases complicated with H. influenzae bacilli, 39 were males and two were females. One hundred and ninety-nine of the 259 remaining cases were males and 50 were females (Table I). This is not considered a valid comparison, however, because of the predominant male population.

The patients in the entire series ranged in age from three months to 53 years, with the majority occurring in young adults between the ages of 17 and 25 years in both the H. influenzae and the other groups (Table II). This figure is influenced by a predominantly military population.

Symptomatology and Physical Findings

No significant difference in the mode of onset or the length of illness prior to admission was noted in the two groups. Over two-thirds of all patients had been ill less than a week at the time of their admission. In most of them the onset of illness was gradual. Upper respiratory infection

TABLE I

H. Influenzae Bac. Cases		41
Male	39	
Female	2	
All Other Cases		259
Male	199	
Female	60	
TOTAL CASES		300

TABLE II

Age	H. Influ. Group	Control
0 to 5	2	45
6 to 16	1	21
17 to 30	33	159
Over 30	5	34
TOTAL	41	259

had been present for a few days, followed by the development of malaise, chilliness, fever, cough and chest pain. Twenty-five per cent had been ill for from one week to a month prior to hospitalization, while 3 per cent had been ill more than a month (Table III).

The complaints and symptoms at the time of admission were similar in the two groups. Cough, occurring in over 80 per cent in both groups, was the most common complaint. About 4 per cent had blood-streaked sputa prior to admission. Fever, occurring in over two-thirds of all the patients prior to admission, was the next most common complaint in both groups. The two groups are compared in Table IV.

The initial physical findings were practically the same in the two groups (Table V). Fever was usually present. The most helpful localizing sign was the presence of rales which were found on the initial examination in 45 per cent of the cases. These varied in character but were usually fine and crepitant. Dullness to percussion over the area involved was present in about 20 per cent of the patients. Breath sounds were decreased over the area

TABLE III: DAYS ILL PRIOR TO HOSPITALIZATION

No. of Days	H. Influ. Group Per cent	Control Per cent
1 week or less	65.9	74.3
1 to 2 weeks	17.1	13.7
2 to 3 weeks	9.7	6.0
3 to 4 weeks	2.4	2.7
Over 4 weeks	4.9	3.3
TOTAL	100.0	100.0

TABLE IV: SYMPTOMS PRIOR TO ADMISSION

Symptoms	H. Influ. Group Per cent	Control Per cent
Cough	80.5	82.2
Fever	56.1	79.5
Chest Pain	19.5	30.9
Chilliness	21.9	28.2
Headache	19.5	23.9
Coryza	29.5	22.0
Sore Throat	17.0	12.0
Hemoptysis	2.4	4.3
Dyspnea	7.3	1.9

TABLE V: PHYSICAL EXAMINATION OF CHEST

Findings	H. Influ. Group Per cent	Control Per cent
Negative	26.8	30.5
Breath Sounds, Involved Area,		
Increased	9.7	15.4
Decreased	26.8	18.9
Rales	46.3	44.8
Rhonchi	9.7	15.4
Dullness	21.9	20.5
Friction rub	0	2.3

involved in over 20 per cent, while they were increased in about 15 per cent over the area of pneumonitis later demonstrated by roentgenograms. Coarse rhonchi were heard in about 15 per cent and dyspnea and friction rubs were heard infrequently. In about 30 per cent physical examination of the chest was completely negative, making the diagnosis by physical examination alone impossible.

Laboratory Data

White blood cell and differential counts were done routinely on admission and were repeated on an average of once a week during the patients' hospital stay. Taking the highest values on any of the counts, it was found that 67.6 per cent of all the control patients had normal total white blood cell counts ranging between 5,000 and 10,000 cells, while those complicated with H. influenzae bacilli showed 58.5 per cent with counts between 5,000 and 10,000 cells (Table VI). Generally, however, patients in the control group who showed high white counts were mostly below the age of two years. In those patients on whom erythrocyte sedimentation rates were measured, it was noted that this was elevated in the majority in both groups of patients.

Sputum cultures were carried out routinely on all 300 patients. Hemophilus influenzae bacilli were recovered in moderate to abundant growth in 41. Of those organisms typed, it was found that none was type B, and there was no predominance in any of the other types. These cases represent 13.7 per cent of the entire series. In 80 cases (26.6 per cent) beta hemolytic streptococci were recovered from the sputa. The clinical course in the group showing beta hemolytic streptococci was no different than the course in those patients showing only normal flora in the sputum. In 60 per cent of the cases a normal flora, consisting mainly of Neisseria catarrhalis and alpha hemolytic streptococci, could be grown from the sputa (Table VII).

Hospital Course

A definite difference in the two groups of patients is noted in the duration of hospitalization. In the H. influenzae bacillus group this varied from three to 53 days, with an average of 16.7 days per patient, whereas the

TABLE VI: WHITE BLOOD CELL COUNT

Count	H. Influ. Group Per cent	Control Per cent
5-10,000	58.5	67.6
10-12,000	7.3	6.6
12-15,000	17.1	9.9
15-20,000	7.3	9.7
Over 20,000	9.8	6.2

TABLE VII: SPUTUM CULTURE

Organism	No. of Cases
H. Influenzae Bacilli	41
Beta Hem. Streptococci	80
Normal Flora	179

control group varied from three to 45 days with an average hospitalization of only 11.6 days per patient (Table VIII). Over 75 per cent of the control group were discharged from the hospital after a stay of two weeks or less, while less than 55 per cent of the H. influenzae bacillus group were out of the hospital after an equal period of time. About 5 per cent of the control group had a hospitalization of more than one month while over 12 per cent of the H. influenzae bacilli cases required more than a month's hospitalization.

A difference between the two groups was also noted in the severity and duration of fever. These in the H. influenzae bacillus group ran an oral temperature of over 100 degrees F. for an average of 3.3 days, while the control group averaged only 2.0 days. Over 22 per cent of the control group had no temperature above 100 degrees F. while 17 per cent of the H. influenzae bacillus group remained below 100 degrees F. Almost 15 per cent of the H. influenzae bacillus group ran a fever of 100 degrees F. from seven to 10 days, while only about 2 per cent of the other patients ran fevers for that length of time (Table X). The majority in both groups showed fever peaks between 100 and 102 degrees F. during the febrile period, but occasionally some would run fevers as high as 105 degrees F. The high fevers were seen much more frequently in the H. influenzae bacillus group.

Chest roentgenograms, including poster-anterior and lateral views, were taken on all patients on admission to the hospital. Most of them had pneumonitis in more than one lobe. The lower lobes were involved in about 50 per cent of the cases, the right middle lobe in about 25 per cent, the lingula in about 25 per cent, and each upper lobe in about 9 per cent. There was no essential difference noted by x-ray film inspection between the control group and the H. influenzae group (Table IX).

TABLE VIII: CHEST ROENTGENOGRAMS

Lobes	H. Influ. Group Per cent	Control Per cent
RUL	7.3	10.0
RML	31.7	23.9
RLL	51.2	50.2
LUL	7.3	9.2
Ling.	29.2	22.0
LLL	68.3	47.5

TABLE IX: DAYS OF HOSPITALIZATION

Days	H. Influ. Group Per cent	Control Per cent
3-6	7.3	23.5
7-9	19.5	27.4
10-12	19.5	18.5
13-14	7.3	6.9
15-21	24.4	14.3
22-28	9.8	4.3
29-35	4.9	3.5
36-53	7.3	1.6
Average	16.7 Days	11.6 Days

Approximately 51 per cent of the H. influenzae bacillus group and 48 per cent of the others were discharged from the hospital with some residuals of pneumonitis still present by roentgenograms. They were clinically well and repeat x-ray films, plus follow-up studies after discharge, revealed further clearing or complete resolution in most of the cases, except as noted below. Most of the patients in both groups improved subjectively and clinically before their x-ray films showed clearing of the pneumonitis.

Over 21 per cent of the control group showed complete clearing by x-ray film inspection within one week as compared to about 12 per cent in the H. influenzae bacillus group. However, at the end of two weeks the percentage of patients with normal x-ray films was approximately the same in the two groups (Table 11).

Complications

The most frequent complication seen in both groups was the development of pleural fluid. There were four cases in the H. influenzae bacillus group

TABLE X: DAYS TEMPERATURE OVER 100 DEGREES F.

No. of Days	H. Influ. Group Per cent	Control Per cent
0	17.0	22.4
1	19.8	29.3
2	12.2	14.7
3	7.3	13.9
4	14.6	8.5
5	4.8	6.9
6	9.7	1.9
7-10	14.6	2.3
Average	3.3 Days	2.0 Days

TABLE XI: ROENTGENOGRAMS CLEARED

Time	H. Influ. Group Per cent	Control Per cent
1 week	12.2	21.6
2 weeks	29.2	22.0
3 weeks	4.9	5.7
4 weeks	0.0	2.3
8 weeks	2.4	0.4
Residual on Discharge	51.3	48.0

TABLE XII: COMPLICATIONS

	H. Influ. Group Per cent	Control Per cent
Pleural Effusion	9.8	4.2
Blunting	4.9	2.3
Mod.-Marked	2.4	1.9
Empyema	2.4	0.0
Pneumothorax	0.0	0.4
Lung Abscess	0.0	0.4
Marked Atelectasis	0.0	0.8
Relapse	19.5	1.5
Extension of Pneumonia	12.2	0.8

and 11 in the control group, corroborated by x-ray film inspection. Two of the cases in the H. influenzae bacillus group showed massive effusion requiring thoracentesis and the latter one, a patient of nine months, had empyema from which H. influenzae bacilli were recovered in pure culture. In the control group, a spontaneous pneumothorax was seen in one case, a lung abscess developed in another, and areas of extensive atelectasis were observed in two.

Sixty Army recruits were returned to duty clinically recovered and fully ambulatory but with slight residuals of pneumonitis demonstrable by x-ray film. Twelve of them (20 per cent) returned to the hospital with clinical relapses, seven of whom had x-ray film evidence of extension to areas of lung other than those involved at the time of the first hospitalization. Of these 12, eight (19.5 per cent) were in the H. influenzae bacillus group, as compared to 1.5 per cent in the control group.

Treatment

Of the 259 cases of primary atypical pneumonia in this series, uncomplicated by H. influenzae bacilli, 129 (49.8 per cent) were treated with symptomatic measures only. They were kept at bed rest with bathroom privileges until their temperatures had been normal for at least 48 hours. Salicylates were used to control fever and general malaise. The remaining 130 (50.2 per cent) patients received various antibiotics in addition to the symptomatic measures. Fifty-one (19.6 per cent) were treated with aureomycin, 2 Gm. daily; 13 (5 per cent) received chloramphenicol, 2 Gm. daily; while 66 (25.5 per cent) received a course of penicillin, usually 300,000 to 600,000 units daily.[10-12]

In general, patients receiving the antibiotics were those who appeared more ill clinically at the time of admission or those who failed to recover as rapidly as the members of the group receiving symptomatic measures only.

This is not a strictly controlled series, but it is our impression that penicillin has no demonstrable effect in shortening the clinical course, reducing fever, or symptoms. In some aureomycin and chloramphenicol did appear to give beneficial results in reducing the temperature to within normal limits and giving symptomatic improvement.[10,11] These two antibiotics, however, were not effective in shortening the total course of resolution of the pneumonitis.

In the H. influenzae bacillus group 26 (63.4 per cent) were treated with antibiotics, particularly those who demonstrated the more severe signs and symptoms. Six (14.6 per cent) received aureomycin, 2 Gm. daily; eight (19.5 per cent) received chloramphenicol, 2 Gm. daily; and 12 (29.2 per cent) received penicillin, 300,000 to 600,000 units daily.

Penicillin had no noticeable effect when used in maximal doses up to five days. When aureomycin and chloramphenicol were used, either after a period of observation or following a trial period on penicillin, there was a prompt temperature fall and symptomatic improvement. Malaise improved and sputum cultures cleared; however, the x-ray films did not show faster

resolution than in the remainder of patients in the series. There were a few from whom H. influenzae bacilli were cultured in abundant growth, yet their clinical course could not be differentiated from the milder, uncomplicated cases of the non-Hemophilus group, indicating, perhaps, that some patients are more susceptible to this organism than others.

Recurrence

The recurrence rate was high in the H. influenzae group by bacteriological examination, and clinical and radiographic findings. This indicated that the drugs were only bacteriostatic, and that the patient's resistance in many cases was low.

SUMMARY

A series of 300 cases of primary atypical (viral) pneumonitis is presented in two groups. One group of 41 showing H. influenzae bacilli by culture of the sputa is compared to a group of 259 which failed to grow this organism on culture. It appears from this study that H. influenzae bacilli as a secondary invader is likely to produce a more severe and prolonged illness than the viral pneumonias which have no secondary bacterial infection. It appears that aureomycin and chloramphenicol are effective in producing subjective and clinical improvement in these patients, but do not seem to hasten resolution of the pneumonitis.

RESUMEN

Se presentan una serie de 300 casos de neumonitis atipica de virus en dos groups. Un grupo de 41 casos, en el que se encontró el bacilo hemófilo de la influenza en los esputos, es comparado con otro grupo de 259 que los que no se obtuvo cultivo de este organismo. Según este estudio, parece que bacilo hemófilo de la influenza, es un invasor secundario que posiblemente produce una enfermedad más prolongada y severa que las infecciones a virus que no tienen esa asociación. Parece que la aureomicina y el cloramfenicol, son efectivos para producir mejoría clínica en estos enfermos, pero no parece que apresuren la resolución de la neumonitis.

RESUME

Les auteurs présentent en deux groupes une étude de 300 cas de pneumonie primaire atypique à virus. Ils comparent un groupe de 41 malades, ayant des bacilles de Pfeiffer à la culture des crachats au groupe de 259 malades chez lesquels ces bacilles n'ont pas été retrouvés.

Il découle de cette étude que les bacilles de Pfeiffer agissant comme agents d'infection secondaire sont susceptibles de créer une affection plus sévère et plus longue que lorsque la pneumonie à virus n'est pas compliquée d'infection secondaire. Il semble que l'auréomycine et la chloromycétine sont efficaces, et produisent une amélioration clinique et subjective chez les malades, mais ces produits ne semblent pas hâter l'évolution de la pneumonie.

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The Use of Nitrogen Mustard in Advanced Bronchogenic Carcinoma*

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Carcinoma of the lung and bronchial tree is currently receiving much attention in both professional and lay publications. Recent developments in both diagnosis and surgical therapy have shown that real hope lies in diagnosis made before onset of symptoms and in earlier resection.

O'Loughlin and Tucker[1] have found a "silent period" of five to 19 months between roentgen signs of disease and the onset of symptoms. There is ample reason to believe that it is now possible to discover many lesions at an early stage with consequent earlier resection and a much improved surgical cure rate. Overholt believes this cure rate could be as high as 75 per cent in the early cases.

For the present, however, we are faced with a large number of surgical incurables. While the long term prognosis for these patients is not good, advances in radiation therapy and in chemotherapy justify an energetic program of palliation. Real benefit may now be offered in a material number of cases. This benefit will be manifest both in relief of distress and in prolongation of fairly comfortable life.

Present techniques indicate that the best palliation may be obtained by use of both radiation and chemotherapy. Many cases, however, are not suitable for radiation and here we must rely on chemotherapy alone.

The agents most effective to date in the chemotherapy of cancer are the nitrogen mustards. This report concerns results obtained using nitrogen mustard in the palliation of unresectable carcinoma of the lung and bronchial tree. Since 1948, 56 such cases have received this therapy at the Veterans Administration Hospital, New Orleans, Louisiana, and form the basis of this report.

Method of Administration

Nitrogen mustard was given intravenously in doses of 0.1 mgm. per kilogram of body weight, once daily for four consecutive days in most of the reported cases. Nausea and vomiting resulted after therapy in the majority of the cases; in those patients whose symptoms were severe the daily dose was reduced to one-half that above and therapy continued eight to 10 days. This usually resulted in a marked reduction of undesirable symptoms. Nitrogen mustard is a systemic toxin with special selectivity for the blood

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forming organs and actively proliferating tissue. As a result leukopenia, thrombocytopenia, anemia and bone marrow depression were common findings after therapy.[3-5] Fresh blood transfusions, antibiotics and chemotherapy were useful adjuncts in combating the toxic effects of a damaged hematopoietic system.

Results

Definite benefit of such degree as to materially alleviate symptoms and apparently to prolong life was obtained in 15 cases (27 per cent). In two of these patients, evidence of improvement lasting for nine and 10 months respectively was observed. Three others had benefit extending over a five month period in each case (See Tables I and II).

Subjective evidence of improvement consisting of such factors as decrease in chest pain, dyspnea, anorexia, weakness, cough and fever was frequently observed (See Table III).

Objective evidence of improvement was less striking but was observed in a significant number of cases. Eleven patients (20 per cent) revealed objective evidence by one of the following criteria: decrease in superior vena cava syndrome (three cases), weight gain, decrease in size of pulmonary lesion, resolution of pleural fluid, regression of metastases and regression of obstructive pneumonitis (See Table IV).

Three of the patients with histologically undifferentiated carcinoma received two courses of therapy followed by considerable benefit after both courses. Undifferentiated tumors also showed greatest response as measured by length of life following therapy. The greatest response in this class of

TABLE I

RESPONSE ACCORDING TO HISTOLOGY (56 cases)

Type	No Benefit	Slight Benefit	Definite Benefit
Undifferentiated	14	7	6
Squamous cell	8	3	5
Adenocarcinoma	7	0	2
Oat cell	1	1	1
Alveolar cell			1

TABLE II

DURATION OF DEFINITE BENEFIT (15 cases)

Type	1-3 Month Benefit	3-6 Month Benefit	Over 6 Months Benefit
Undifferentiated	3	2	1 (9 Mos.)
Squamous cell	3	1	1 (10 Mos.)
Adenocarcinoma	2	0	
Oat cell	1	0	
Alveolar cell	1	0	

tumors is in accord with previous observations that sensitivity to nitrogen mustard is roughly parallel to sensitivity to irradiation.[6]

The duration of life following nitrogen mustard therapy reveals that 13 patients (27 per cent) survived six to 12 months, while three (6 per cent) lived over 12 months. The average duration of life of all cases was four months after treatment.

Of incidental interest is response for one month of a case of alveolar cell carcinoma. It has been previously recorded that this tumor does not respond to mustard.

Case Reports

Case 1: B.J.S. No. 12276. A 52-year old white man entered the Veterans Administration Hospital, New Orleans, Louisiana, on February 8, 1949, with the diagnosis of bronchogenic carcinoma with metastasis to a left supraclavicular node. Biopsy of this node revealed anaplastic carcinoma. On admission, he presented evidence of superior vena cava syndrome manifested by swelling of his face and neck which became more pronounced after lying down, dyspnea, dysphagia, pain in the right shoulder and arm, dizziness, weakness, fatigue, increased lacrimation of both eyes, decreased visual acuity and mild cough. X-ray film revealed a dense mass in the right paratracheal region, extending into the anterior mediastinum with compression on the apical branch of the right upper lobe bronchus and partial compression of the trachea (Figure 1). On February 21, 1949, a course of nitrogen mustard was begun with immediate improvement: i.e., decrease in dyspnea, ability to sleep flat in bed, less pronounced swelling of face and neck on arising in the morning, disappearance of pain, dysphagia, lacrimation and throbbing sensations in head. Objective signs of improvement included decrease in telangiectasia on anterior thorax and decreased venous pressure in arms from 380 mm. to 310 mm. of water. X-ray film of the chest on March 3, 1949 (11 days after beginning of HN_2) revealed marked reduction in the size of the superior mediastinal mass on the right. It extended 1.5 cm. less in the lateral direction and impinged less upon the trachea.

TABLE III

SUBJECTIVE IMPROVEMENT (26 cases)

Symptom	Number Showing Response
Chest pain	19
Dyspnea	15
Anorexia	15
Weakness	14
Cough	14

TABLE IV

OBJECTIVE IMPROVEMENT (11 of 25 cases)

Objective Finding	Number Showing Response
Superior vena caval obstruction	*3
Gain in weight	4
Decrease of pulmonary lesion	3
Resolution of pleural fluid	2
Regression of metastases	1
Regression of obstructive pneumonia	1

* Three of nine cases with superior vena cava obstruction responded.

The inferior mediastinal widening, including that seen on the left, was also markedly reduced. The fluid in the right hemithorax had been absorbed (Figure 2).

Case 2: R.J. No. 19366. A 58-year old colored man complained of weight loss and hemoptysis in November, 1946. Left pneumonectomy was done for adenocarcinoma of bronchus at the New Orleans Charity Hospital in January, 1947. This was followed by x-ray therapy and he was relatively asymptomatic. He regained his normal weight of 185 pounds. Three years later there was onset of burning pain and swelling of left breast, weight loss and dyspnea. He then received further x-ray therapy to the left chest. On admission to the New Orleans Veterans Administration Hospital a large tumor mass measuring 10 x 8 x 5 inches was present in the region of the left breast which extended with a nipple-like projection laterally. Following HN_2 therapy the tumor mass decreased in size for three weeks and pain was relieved for four weeks. The tumor mass later increased in size and he expired on December 17, 1950.

This tumor was diagnosed and operated early and he was apparently cured for three years. Nitrogen mustard therapy produced temporary improvement of metastatic skin lesions.

Discussion

It is believed that the preceding observations show nitrogen mustard to be a palliative agent of definite value in nonoperable carcinoma of the lungs and bronchi. The present study also indicates that results are gener-

FIGURE 1. Case 1: Chest x-ray film made prior to nitrogen mustard therapy. Note superior mediastinal mass on right.

ally inferior to those obtained by radiation therapy. Nitrogen mustard will probably find its greatest usefulness in the following situations:

1) Superior vena cava obstruction where immediate relief of distressing symptoms must be obtained rapidly.

2) Further palliation where maximum benefit has been obtained by previous radiotherapy or palliative resection.

3) Relief of pain from widespread metastases.

4) Nitrogen mustard therapy may occasionally make possible the application of radiotherapy in situations where it would not otherwise be feasible.

SUMMARY

1) Nitrogen mustard is a valuable adjunctive agent for therapy of inoperable bronchogenic carcinoma.

2) Benefit was obtained in 46.5 per cent of cases studied in this series.

3) The agent is particularly valuable where superior vena cava obstruction must be relieved rapidly. Histologically undifferentiated cells showed the most marked response.

4) The attitude that there is little to be gained from palliation is incorrect.

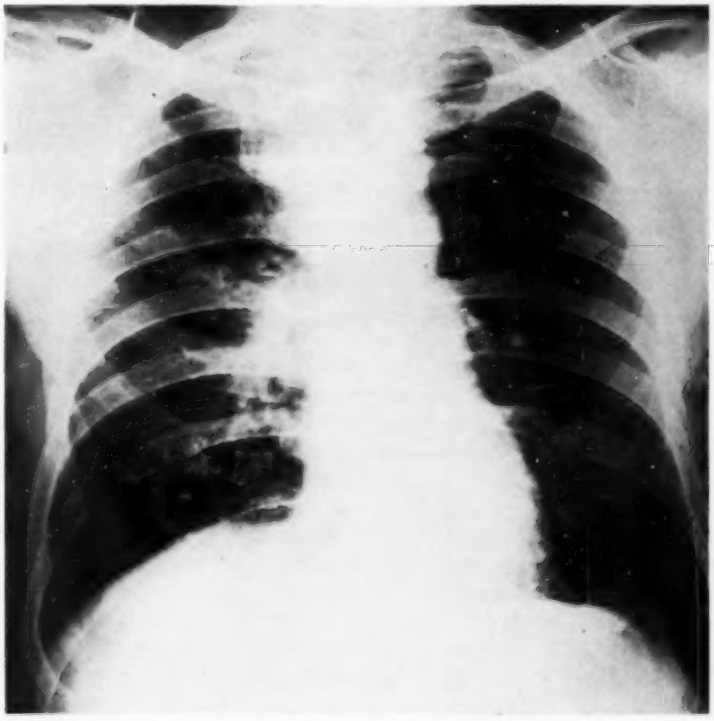

FIGURE 2. Case 1: Chest x-ray film made following nitrogen mustard therapy. Note regression of tumor mass.

RESUMEN

1) La mostaza nitrogenada es un valioso adypvante para el tratamiento del carcinoma bronquigénico inoperable.

2) Se obtuvo beneficio en el 46.5 por ciento de los casos estudiados en esta serie.

3) El agente es particularmente valioso cuando la compresión de la vena cava superior debe aliviarse rapidamente. Histológicamente las celdillas no diferenciadas mostraron la respuesta mas marcada.

4) La actitud que sostiene que poco puede ganarse con la paliación es incorrecta.

RESUME

1) Le gaz moutarde est une thérapeutique d'appoint de grande valeur dans les cancers bronchiques inopérables.

2) Dans 46.5% des cas étudiés, dans une série rapportée par les auteurs, les malades en tirèrent avantage.

3) Ce produit est particulièrement efficace quand il est nécessaire de supprimer rapidement une obstruction de la veine cave supérieure. Ce sont les cancers à cellules indifférenciées qui sont les plus sensibles à ce traitement.

4) L'idée qu'un traitement palliatif ne donne que peu d'avantages ne peut se soutenir.

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Tuberculin Reactors in the General Population

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Grand Rapids, Michigan

Tuberculin testing as a part of case-finding programs and as an aid in differential diagnosis has become increasingly important in recent years. Formerly the test was little used because it was the general belief that all adults and the majority of children living in urban communities were infected with tubercle bacilli. Veeder and Johnston[1] (1915), noted statements were frequent in medical and lay literature to the effect that 90 per cent or more of children are infected with tubercle bacilli by the 14th year. In tracing the authority for such statements, they found them based almost entirely on the figures of Hamburger and Monti[2] who, in 1909, reported the results of tuberculin tests on 532 children convalescing from diphtheria and scarlet fever in the wards of a public hospital in Vienna. The figures ranged from 9 per cent reactors at one to two years to 94 per cent reactors at 13 to 14 years. VonPirquet[3] reported (1909) the results of tuberculin tests on 1,407 children (including cases of clinical tuberculosis). His figures ranged from 20 per cent reactors at one to two years to 80 per cent at 10 to 14 years. The figures of both Hamburger and VonPirquet were obtained from tests on children of the poorer classes of society in Vienna.

Veeder and Johnston (1915), published the results of the VonPirquet cutaneous test on 1,321 children admitted to a hospital (over a period of three years) from the poorer and more congested districts of St. Louis. These were admitted for various causes, including clinical manifestations of tuberculosis. They found reactors ranging from 24 per cent at one to two years to 54 per cent at 12 to 14 years. When those with clinical tuberculosis were excluded the percentage of reactors in the 10 to 14 year age period was only 43 per cent.

Slater,[4] in 1924, found only 10 per cent reactors to the VonPirquet test among 1,654 unselected school children, ages six to 16 plus years, in a relatively wealthy farming section of Minnesota. In 1931 he reported 10.4 per cent reactors among a similar group tested with 0.1 mgm. of old tuberculin by the Mantoux method.

In 1935 Aronson[5] presented the results of a survey of the white population of six rural Michigan counties. The report included the rural sections of Kent County. He used old tuberculin intradermally, 0.01 mgm., followed 48 hours later by 1 mgm. in those who did not react to the first dose. Among the 8,025 persons tested reactors ranged from 6.1 per cent under five years, 17.8 per cent at 10 to 14 years, to 76.4 per cent at 40 years and over. It should be noted that the figures for Kent County alone were somewhat

*From the Sunshine Sanatorium, Grand Rapids, Michigan.
I gratefully acknowledge the assistance of Miss Gladys Meengs of the Kent County Tuberculosis Society in gathering material for this study.

TABLE I

Age	TUBERCULIN 0.01 mgm., 1950 Number Examined	Number Positive	Percent Positive	TUBERCULIN 0.1 mgm., 1951 Number Examined	Number Positive	Percent Positive
0 to 10	2	1	50	2,069	6	.29
10 to 20	132	7	5.3	3,808	134	3.5
20 to 30	1,172	199	17	1,651	298	18
30 to 40	1,178	344	29.2	992	314	31.6
40 to 50	718	326	45	694	357	51.5
50 to 60	311	182	58.5	481	319	66.3
60 to 70	139	77	55.4	211	140	66.3
70 to 80	25	14	56	58	34	58.6
80				5	0	0
TOTAL	3,677	1,150		9,969	1,602	

TABLE II

PERCENT OF TUBERCULIN REACTORS BY AGE GROUP

	Test	Date	Locality	Number Tested	10-19 yrs. per cent
Hamburger and Monti	Cutaneous and Subcutaneous	1909	Vienna	532	43
VonPirquet	VonPirquet	1909	Vienna	1,407	31
Veeder and Johnston	VonPirquet	1915	St. Louis, Missouri	1,321	30
Slater	VonPirquet	1924	Minnesota	1,654	9.8
Aronson	Mantoux	1933	Kent Co., Michigan	1,761	10
Aronson	Mantoux	1933	6 Rural Co., Michigan†	8,025	(0-5, 5-9) 6.1 9.6
Whitney and McCaffrey	1st and 2nd PPD	1934 to 1936	U.S.*	56,688	23
Canada and Babione	0.0001 mgm. PPD	1948	Navy and Marine Recruits	79,393	
Bellomo	Mantoux 0.1 and 1 mgm.		St. Paul, Minnesota	2,000	11
Present Study	Mantoux O.T. 0.1 and 1 mgm.	1950 and 1951	Kent Co., Michigan	21,781	1.9
NUMBER TESTED				4,592	

* Adjusted to age, color, and nationality percentage in population.

lower than the average for the six counties—3.2 per cent five years and under, 18.9 per cent at 10 to 14 years, 71.1 per cent at 40 and over (Table II).

Whitney and McCaffrey[6] (1937), reported a nation-wide survey with PPD (0.00002 mgm., retesting non-reactors with 0.005 mgm.) adjusted according to age, color, nationality and parentage distribution of the population in the United States. They found 47 per cent reactors among 56,688 persons of all ages. Their figures were: five years and under, 24.9 per cent; 10 to 14 years, 28.4 per cent. Canada and Babione[7] found among 79,393 midshipmen,Navy and Marine recruits enlisting in 1948, nearly all of whom were between 17 and 23 years of age, 9.7 per cent reactors to 0.0001 mgm. of PPD.

In 1952 Bellomo[8] published the results of Mantoux tests given 2,000 people seen in private practice in St. Paul, Minnesota. Old tuberculin, 0.1 mgm. and 1 mgm., was used. Reactors varied from 11 per cent in the first decade to 76 per cent in the sixth (Table II).

Material

This study consists of a review of consecutive tuberculin tests given by the Tuberculosis Society of Kent County, Michigan, from March 1 to September 1, 1950, and the corresponding six months of 1951. The purposes of

TABLE II

PERCENT OF TUBERCULIN REACTORS BY AGE GROUP

10-19 yrs. per cent	20-29 yrs. per cent	30-39 yrs. per cent	40-49 yrs. per cent	50-59 yrs. per cent	60-69 yrs. per cent	70-79 yrs. per cent	80-89 yrs. per cent
(10-14) 94							
(10-14) 80							
(10-14) 43							
10.7							
19	41	45.9	(- - -		71.1	- - -	)
(10-14, 15-19) 17.8 26.4	(20-24, 25-29) 41 52.4	61.8	(- - -		76.4	- - -	)
35	(- - - - - - -		60.1	- - - - - - -			)
(17-23) 9.7							
15	38	54	66	76	71	69	57
7.9	26.8	41.2	(- - - 58.7	71.1	64.4 - - - 71.2	68.1	) 44.4
7,830	3,234	2,641	1,849	1,036	480	110	9

† Saginaw, Iosco, Ogemaw, Kent, Isabella and Ottawa Counties.

the study were (1) to compare the percentage of reactors and number of severe reactors to old tuberculin given intradermally in doses of 0.01 and 0.1 mgm.; (2) to determine the percentage of reactors to these amounts of old tuberculin by age groups in this county.

The old tuberculin used was prepared and supplied by the Michigan Department of Health Laboratories. The tests were given and reactions read after 48 to 72 hours by nurses who have had many years training and experience in the technique. The examinations were done in grade schools, high schools, colleges, factories, stores and on street corners in conjunction with the operation of the Kent County mobile x-ray unit. All persons who presented themselves for examination were tuberculin tested unless it was known from previous Tuberculosis Society, Public Health Clinic or private physician's records of recent years that they were tuberculin reactors. In that circumstance the test was not repeated.

Kent County, Michigan has a population of 288,292 of whom 176,500 live in the City of Grand Rapids. East Grand Rapids has a population of 6,400. Ten thousand reside in five towns of 1,000 to 2,500 each. The remaining 95,000 live in rural sections. There are 7,100 (2.5 per cent) negroes and an occasional Mexican and Indian family. These urban, rural and racial groups are represented in the study in approximately correct proportions.

It had been customary for a number of years and through 1950 to give old tuberculin, 0.1 mgm., to school children and 0.01 mgm. to adults. Through high school age only the tuberculin reactors were x-rayed. All adults received chest films. During the six months of 1951 covered by the study, both children and adults were given 0.1 mgm. of the antigen. In comparing the two dosages, known reactors who were not retested are not included. Five mms. or more of induration was considered positive. During

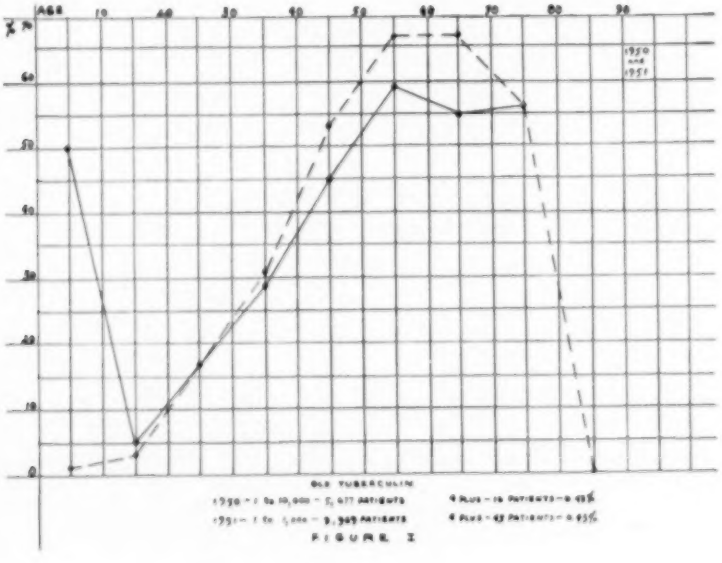


FIGURE 1

the six month period of 1950, 3,677 individuals were given 0.01 mgm. During the same six months of 1951, 9,969 persons were tested with 0.1 mgm. (Table I).

Results

Only two individuals in the first decade of life were tested with 0.01 mgm. One reacted. Five in the ninth decade received 0.1 mgm. None reacted. With these two exceptions, of statistical insignificance, the curve of the percentage of reactors is 1 to 11 per cent higher with 0.1 mgm. in the third, fourth, fifth and sixth decades (Table I and Figure 1). It is interesting to note that four plus reactions (necrosis) were recorded in 0.43 per cent of the persons in each group: 16 of 3,677 and 43 of 9,969 tested.

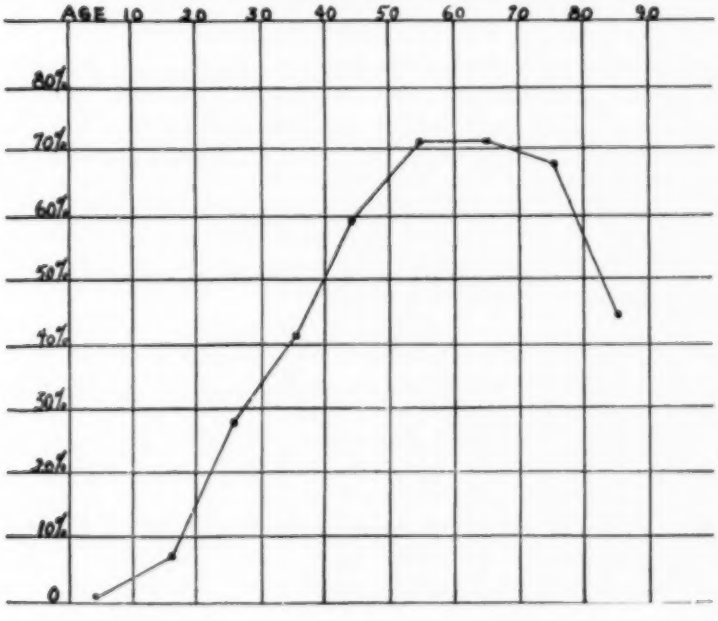
For the purpose of approximating the percentage of tuberculin reactors in the general population, all persons presenting themselves for examination during the six month period of both years were included.

1,757 — already known to be reactors.
3,677 — 0.01 mgm. O.T. in 1950.
6,378 — 0.1 mgm. O.T. in 1950 (school children).
9,969 — 0.1 mgm. O.T. in 1951.

21,781 — Total.

FIGURE II

21,781 Tuberculin Tests
1950 – 1951
Percent Reactors by Decade



Those who were known reactors from previous years had been tested with either 0.1 mgm. or 0.01 mgm. It is seen, then, that upwards of 75 per cent of the individuals included in this study received the 0.1 mgm. dose.

There were 1.9 per cent reactors in the first decade of life; 7.9 per cent in the second, and a peak of 71.2 per cent in the seventh (Table II and Figure 2). In the eighth and ninth decades the percentage of reactors decreased.

Discussion

There was a preponderance of school children in the total number tested. Therefore the average 22.5 per cent reactors in the entire group tested cannot be accepted as the average for the population of the community. Doubtless the curve for all ages would be somewhat higher if non-reactors had been re-tested with 1 mgm. of the antigen. In our general case-finding work we have not found re-testing practical.

The percentage of reactors under 30 years of age is definitely lower, but after 30 years differs very little from the findings in rural Kent County in 1933. The two studies, however, are not comparable. The present study includes both urban and rural communities. Aronson studied rural communities only and re-tested non-reactors with 1 mgm. old tuberculin.

SUMMARY

Old tuberculin (0.01 mgm.) was administered intradermally to 3,627 persons and 9,969 were similarly tested with 0.1 mgm. The percentage of reactors to each dose was compared according to the decade of life. The percentage of reactors was 1 to 11 per cent higher with the larger amount of antigen.

Of the patients tested with each strength dose, 0.43 per cent were reported as showing four plus reaction.

In Kent County, Michigan, 21,781 were tested with tuberculin and/or had x-ray films of their chests in corresponding six month periods in 1950 and 1951. There were 1,757 who were already known by a record of previous examinations to be tuberculin reactors. There were 3,677 tested with 0.01 mgm. old tuberculin and 16,347 with 0.1 mgm. Among the 21,781 who were tested, 1.9 per cent of those in the first decade of life and 7.2 per cent in the second decade reacted to the tuberculin.

RESUMEN

Se administró tuberculina antigua a la dosis de 0.01 intradérmica a 3,627 personas y otras 9,969 fueron probadas con la dosis de 0.1 de miligramo.

El porcentaje de reactores a cada dosis fué comparado de acuerdo con la década de su vida. El porcentaje de reactores fué de 1 a 11 por ciento mayor con la cantidad mas grande antigeno.

Entre los enfermos probado con cada dosis, 0.43 por ciento fueron señalados como teniendo una reacción de plus 4.

En el Condado de Kent, Michigan, 21,781 personas fueron probados con

tuberculina y/o se hicieron peliculas del torax en periodos de seis meses en 1950 y 1951.

Hubo 1,757 que ya se sabia de antemanos por pruebas anteriores que eran reactores a la tuberculina. 3,677 fueron probados con 0.01 mg. de O.T. y 16,347 con 0.1 mg. Entre los 21,781 que se encontraban en la primera década de la vida 1.9 por ciento reaccionaron a la tuberculina y solo 7.2 por ciento de aquellos que se encontraban en la segunda década. En tanto que aquellos en su septima década reaccionaron en el 71.2 por ciento.

RESUME

L'auteur à utilisé des injections intra-dermiques de 0.01 mmgr. de tuberculine brute sur 3,627 personnes, et de 0.1 mmgr. pour 9,969 personnes. Le pourcentage des réactions positives pour chaque dose utilisée a été comparé en fonction de l'âge. Avec la plus forte dose, le pourcentage des réactions positives fut de 1 à 11% plus élevé.

Parmi les malades pour lesquels on essaya chacune des concentrations, 0.43% se montrèrent atteints d'une réaction très forte. Dans le Comté de Kent (Michigan) 21,871 personnes subirent un test tuberculinique, avec ou sans radiographie thoracique, dans les six mois correspondants en 1950 et 1951. Parmi ces personnes, 1,757 individus étaient déjà connus pour avoir une réaction tuberculinique positive. 3,677 individus reçurent de la tuberculine brute, à 0.01 mmgr. et 16,347 de la tuberculine à la dose de 0.1 mmgr. Parmi ces 21,871 individus, ceux qui étaient dans la première décade de leur vie se montrèrent allergiques dans une proportion de 1.9%, et dans la deuxième décade, de 7.2%. Parmi ceux qui étaient dans la septième décade, 71.2% réagirent.

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Teaching Chest Disease

Class Session — The Patient As A Teacher

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Buffalo, New York

The use of individual patients to present material which is ordinarily covered in routine lectures can add human interest and drama which render it memorable.

A great deal of attention today is directed toward visual aids in education. We often overlook or underemploy the most dramatic of visual aids—the patient. In class sessions, the "case presentation" usually consists of wheeling the patient into the room, anxious and embarrassed, while a student or house officer recites the facts of the case in a dry monotonous manner. One or two questions may be directed to the patient and then he is wheeled out of the room. The instructor then attempts to impress the group with the important aspects of the illness of the patient with whom there has been little or no personal contact by most of the members of the audience.

A successful alternative to this has been to allow the patient himself to present the material. We have had the greatest success with this method in teaching certain aspects of pulmonary tuberculosis.

Our patient-teacher has been a middle aged woman who has spent seven years, intermittantly, under sanatorium care. She has developed the missionary zeal of an arrested case of tuberculosis and tells her story with color and enthusiasm. Fortunately, her story in itself is quite colorful.

Her parents died of pulmonary tuberculosis. When her first symptoms occurred, she was refused roentgen examination because she "looked too healthy". At the time the disease was diagnosed, her husband (an alcoholic) was in jail, she was 1,000 miles from home, and her two small children were without care. Hospitalization involved the handling of all those problems. Her boys were placed in foster homes. Her treatment in various sanitoria aroused many different emotional responses, engendered by several physicians and circumstances, which she discusses with candor and feeling.

Finally, after her discharge from the hospital she entered what has been a successful period of rehabilitation. She now supports herself and her sons. As a climax of her discussion, she generally presents to the class her two sons whose health she considers her reward for many years of cooperation with the treatment of her disease.

This is not a scientific presentation. It is a human interest story, which has never yet failed to evoke spontaneous applause from the class. Perhaps it is the extreme contrast with the general medical school lectures that

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The fifth in a series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians.

makes such a profound impression on the students. Whatever the cause, the effect is real. It does a great deal to interest the students in many of the aspects of the disease introduced less successfully in scientific lectures. It emphasizes the importance of early roentgenologic examination, the emotional reaction of the patient on first learning of the disease, the social complications of tuberculosis, the importance of contact examination, the value of rehabilitation, the psychiatric aspects of a patient with this disease, and, above all, the important place of the physician and his attitude at all stages.

These are things we are constantly reminded should be taught more effectively in medical schools today. In this case the patient is a superior teacher.

It is important to point out, however, that this presentation has improved with each year as the patient better understands what aspects of the disease should be emphasized. A presenation of this sort requires as much preparation and organization as any other formal lecture.

To accomplish a successful teaching session the patient must be chosen with care. She should be carefully briefed on what points need emphasis.

She needs encouragement to present her experiences and feelings quite frankly. Finally, she should be encouraged to seek questions and points of view from the students themselves.

This same method of presentation can easily be adapted for other types of pulmonary disease.

Report of the Committee on Scientific Program

In this issue of DISEASES OF THE CHEST we are giving you a preview of the program being arranged by the Committee on Scientific Program for the 20th Annual Meeting of the American College of Chest Physicians, to be held in San Francisco, California, June 17-20, 1954.

Some sections of the program have not as yet been completed and additional speakers will be listed in future issues of the journal. The committee, however, regrets that there will not be sufficient places on the program to accommodate all of the College members as well as other physicians who have submitted titles and abstracts of their papers. It is hoped that these physicians will attend the meeting and participate in the discussions.

Our Committee has had a difficult task in selecting the best papers from the many titles submitted and we are certain that the College members will enjoy another outstanding scientific program this year.

We have been informed that San Francisco will be hard-pressed to take care of all the physicians and their families who will attend the meetings in that city this June. We therefore urge that *you write today* to the San Francisco Convention Bureau, 200 Civic Auditorium, San Francisco 2, and request your hotel reservations. The Fairmont Hotel, which is one of the finest hotels in San Francisco, will be the College headquarters. Nearby are the Mark Hopkins and Huntington hotels and when writing to the Convention Bureau it may be advisable to give your first, second, and third choice of these hotels. San Francisco also has a number of small first class hotels within walking distance of the Fairmont Hotel. If you will write promptly for reservations, we feel certain that all members of the College who wish to attend our meeting will be accommodated.

Edgar Mayer, Chairman	Hurley L. Motley
Herbert C. Maier	Arthur M. Olsen
Arthur M. Master	Reginald H. Smart
Herman J. Moersch	Harold G. Trimble

PRELIMINARY SCIENTIFIC PROGRAM

The Scientific Assembly of the 20th Annual Meeting of the College will open on Thursday evening, June 17, at 8:00 p.m. We are pleased to announce that Dr. Evarts A. Graham, Bixby Professor Emeritus of Surgery, Washington University School of Medicine, St. Louis, Missouri, will present the first paper. Dr. Graham will give the "J. J. Singer Lecture" which is sponsored by the California Chapter of the College. His title will be "Remarks on the Etiology of Bronchogenic Carcinoma".

PANEL ON RESEARCH PROBLEMS

"The Hematological Role of the Lung,"
Howard R. Bierman, Duarte, California.

"Lung Biopsy in Diffuse Pulmonary Disease,"
Peter A. Theodos, Philadelphia, Pennsylvania.
Discussor: Frank Gerbode, San Francisco, California.

"Physiological Effects of Exsufflation with Negative Pressure,"
G. J. Beck and L. Scarrone, New York, New York.
Discussor: Maurice S. Segal, Boston, Massachusetts.

"Mechanism of Cardiac Ascites—An Experimental Study,"
Ivan D. Baronofsky and Joseph L. Sprafka, Minneapolis, Minnesota.

"Bacteriophage Susceptibility of Variant Strains of BCG and Other Tubercle Bacilli,"
Seymour Froman, Irving Krasnow, Drake W. Will and Emil Bogen, Olive View, California.

'Esophageal Motility Studies,"
N. C. Hightower, Temple, Texas.

TUBERCULOSIS

"A Comparative Study on Conventional Therapy vs. Drugs Plus Surgery in Pulmonary Tuberculosis,"
A. R. Allen, et al, Seattle, Washington.

"The Handling of the Poor Risk Patient with Pulmonary Tuberculosis with Reference to Antimicrobial Therapy—Pulmonary Function and Surgery,"
John B. Grow, Sidney Dressler, et al, Denver, Colorado.

"Long Time Antimicrobial Therapy Without Collapse—300 Cases Treated for One Year or Longer,"
W. J. Steininger and W. Leonard Howard, Northville, Michigan.

Summary Presentations

"A Study of the Effects of Distrycin on Pulmonary Tuberculosis—Especially in Streptomycin or Dihydrostreptomycin Sensitive Patients,"
Harry Shubin, Charles A. Heiken, Allen Glaskin, Edward Pennes and Sushil Chakravarty, Philadelphia, Pennsylvania.

"A Pilot Study of 1595, An Isonicotinic Acid Hydrazide Analogue,"
Sol Katz, Georges F. McCormick, Patrick B. Storey, Angel deLeon, Monroe J. Romansky and Edward E. Marshall Jr., Washington, D. C.

Panel Discussion

When do you *not* use excision therapy in pulmonary tuberculosis:
Emil Bogen, Olive View, California.
J. Maxwell Chamberlain, New York, New York.
Al Daniels, San Francisco, California.
Richard H. Overholt, Brookline, Massachusetts.
Sidney J. Shipman, San Francisco, California.

NON-TUBERCULOUS DISEASES OF THE CHEST

"Supervoltage Therapy of Inoperable Bronchogenic Carcinoma,"
Hugh Hare, Boston, Massachusetts.
Discussor: Hirsch Marks, New York, New York.

"The Treatment of Pulmonary Blastomycosis,"
James D. Murphy, Timothy Takaro and James E. T. Hopkins, Oteen, North Carolina.

"Respiratory Infections Due to Klebsiella Pneumoniae,"
Glenn M. Morris and J. Lewis Yates, Detroit, Michigan.

"Clinical Experience with Pneumoperitoneum in the Treatment of So-Called Hypertrophic Emphysema,"
Andrew L. Banyai and Leon Hirsh, Milwaukee, Wisconsin.

"Survey Cancer of the Lung,"
Katharine R. Boucot and Martin J. Sokoloff, Philadelphia, Pennsylvania.

PHYSIOLOGIC THERAPY AND FUNCTION OF PULMONARY DISEASE

"The Microscopic Structure of the Lung,"
Vernon E. Krahl, Baltimore, Maryland.

"Mechanical Factors Governing Expiratory Obstruction of Air Flow,"
Howard Dayman, Buffalo, New York.

"The Clinical Use of Continuous Nebulization in Bronchopulmonary Disease,"
Robert Denton, Oakland, California.

"Treatment of Pulmonary Emphysema with Aerosolized Bronchodilators and Intermittent Positive Pressure Breathing,"
W. S. Fowler, H. F. Helmholz Jr. and R. D. Miller, Rochester, Minnesota.

"Advances in Inhalational Therapy,"
Maurice S. Segal, Boston, Massachusetts.

CARDIOVASCULAR DISEASES

"Indications for Commissurotomy in Mitral Stenosis,"
George C. Griffith, Los Angeles, California.

"Newer Advances in the Treatment of Coronary Thrombosis,"
Arthur M. Master, New York, New York.

"The Treatment of Shock with Vasopressor Amines,"
John J. Sampson, San Francisco, California.

"The New Hypotensive Agents in High Blood Pressure,"
Robert W. Wilkins, Boston, Massachusetts.

SURGERY

"Papillary Adenocarcinoma of the Lung,"
Richard H. Overholt, Brookline, Massachusetts.

"Surgical Treatment of Pulmonary Coccidioidomycosis,"
Bert H. Cotton and J. W. Birsner, Los Angeles, California.

"Further Experiences with Atrio-Septo-Pexy in the Closure of Interatrial Septal Defects,"
Charles P. Bailey, Philadelphia, Pennsylvania.

"Results of Radical Pneumonectomy in Carcinoma of the Lung,"
Speaker to be announced.

Panel Discussion

"Diagnostic Problems in Thoracic Surgery"

OCCUPATIONAL DISEASES OF THE CHEST

Symposium

"Special Forms of Pulmonary Dust Diseases"
Chairman, Reginald H. Smart, Los Angeles, California.

"Anthracosis,"
G. W. H. Schepers, Saranac Lake, New York.

"Pathology of Diatomaceous Earth Pneumoconiosis,"
William H. Carnes, San Francisco, California.

"Asbestosis,"
Kenneth W. Smith, New York, New York.

"Talc Pneumoconiosis,"
Leonard Greenburg, New York, New York.

"Siderosis,"
Robert Charr, Philadelphia, Pennsylvania.

Panel

Moderator, Edgar Mayer, New York, New York
Clinical Aspects: Robert Charr, Philadelphia, Pennsylvania
Physiologic Aspects: Hurley L. Motley, Los Angeles, California
X-ray Aspects: Eugene Pendergrass, Philadelphia, Pennsylvania
Therapeutic Aspects: Reginald H. Smart, Los Angeles, California
Pathological Aspects: Speaker to be announced.

ROUND TABLE LUNCHEONS

There will be six round table luncheon discussions on various topics held on three days during the meeting, namely, Friday, Saturday and Sunday, June 18, 19 and 20. Some of the subjects to be discussed are listed below; however, addi-

tional subjects as well as the names of the panel participants will be announced in subsequent issues of the journal.

"The Lymphomas"
"Esophageal Disease"
"Indication for Pulmonary Surgery in Infancy and Childhood"
"Anomalies of Pulmonary Vessels and Their Clinical Significance"
"Surgical Treatment of Pericardial Lesions"
"The Evaluation of Low Calorie and Low Fat Diets in Heart Disease"
"Cor Pulmonale"
"The Indications for Surgery in Heart Disease".

1954 PRIZE ESSAY CONTEST

The 1954 Prize Essay Contest, sponsored by the Council on Undergraduate Medical Education of the College, is open to medical students studying for the degree of Doctor of Medicine. Essays may be submitted on any phase relating to the diagnosis and treatment of heart and lung disease. The instructions for the preparation of manuscripts are as follows:

1) Five copies of the manuscript typewritten in English (double spaced) should be submitted to the Committee on College Essay, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, not later than March 15, 1954.

2) The only means of identification of the author shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside enclosing the name and address of the author.

3) A letter from the Dean or Chairman of the Department of Medicine or Surgery of the medical school certifying that the author is a medical student studying for the degree of Doctor of Medicine.

The winner of the contest will be awarded a certificate of merit and a cash award of $250.00. The second and third prize winners will receive certificates of merit.

Members of the College are requested to bring this to the attention of undergraduate medical students.

College Chapter News

HAWAIIAN CHAPTER

On December 21 at the Leahi Hospital, Honolulu, the Hawaiian Chapter of the College was formed with Dr. Hastings H. Walker, Honolulu, Regent of the College for Hawaii, elected as the first President and Dr. William F. Leslie, Hilo, Governor of the College for Hawaii, elected Vice-President. Dr. Frederick L. Giles, Honolulu, was elected Secretary Treasurer.

Dr. Seymour M. Farber, San Francisco, California, Regent of the College, attended the organizational meeting and presented a paper entitled "Cytologic Diagnosis in Diseases of the Chest". The Hawaiian Chapter is the 54th chapter to be approved by the Board of Regents of the American College of Chest Physicians.

ILLINOIS CHAPTER

A joint meeting of the Illinois Chapter of the College and the Chicago Roentgen Society was held at the Sheraton Hotel, Chicago, February 11. Guest speaker was

Dr. Leo G. Rigler, Professor and Chief of the Department of Radiology, University of Minnesota, whose topic was "The Roentgenologic Aspects of Diseases of the Pulmonary Vessels."

PERUVIAN CHAPTER

Dr. Leopoldo Molinari of Lima presided at the 7th Annual Meeting of the Peruvian Chapter of the College held in Lima, December 16-18. The following officers were elected for the ensuing year:

President, Ramon Vargas Machuca, Lima
Vice-President, Angel Luis Morales, Lima
Secretary, Victor Narvaez, Lima
Treasurer, Alejandro Flores Degregory, Lima.

Dr. Vargas Machuca stated that plans will be formulated to present another postgraduate course on diseases of the chest in Lima this year.

Dr. Ovidio Garcia-Rosell, Lima, is Regent and Dr. Max Espinoza Galarza, Lima, is Governor of the College for Peru.

JAPANESE CHAPTER

A meeting of the Japanese Chapter took place in Tokyo, September 5, with 200 doctors in attendance. The following papers were presented by Fellows of the College:

"Bronchogenic Carcinoma,"
Shichiro Ishikawa.

"The Basis and Recent Trend of Collapse Therapy,"
Harutaka Baba.

"Prognosis of Lung Resection,"
Shinobu Miyamoto.

"Study of the Bronchus in Surgery of Pulmonary Tuberculosis,"
Naotsugu Kawai.

Dr. Hidejiro Haruki is President, Dr. Naotsugu Kawai is Vice-President, and Dr. Shinobu Miyamoto is Secretary-Treasurer of the Japanese Chapter. Dr. R. K. Start serves as Regent and Dr. Jo Ono is Governor of the College for Japan.

NEW JERSEY CHAPTER

The winter meeting of the New Jersey Chapter will be held on February 23 at the B. S. Pollak Hospital for Chest Diseases, 100 Clifton Place, Jersey City. The meeting will be devoted to discussion of the subject "Pulmonary Emphysema and Cor Pulmonale" and the following speakers will participate in the program:

"Etiology, Pathogenesis, Physiology, Diagnosis and Medical Management,"
Rejane M. Harvey and M. Irene Ferrer, New York, New York.

"Surgical Considerations,"
Ross J. Simpson, Jersey City, New Jersey.

A general discussion will follow.

ANNOUNCEMENTS

The University of Illinois College of Medicine will sponsor a course on Bronchoesophagology March 22 - April 3, under the direction of Dr. Paul H. Holinger. Interested registrants should write to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

The Institute of Cardiology of Mexico will sponsor a Congress on Cardiology to be held in Mexico City, April 21-24.

College News Notes

Dr. J. Winthrop Peabody, Chief Visiting Consultant at Glenn Dale (Maryland) Sanatorium since 1939, terminated his services in that capacity on August 31 in order to devote more time to his private practice and various organizational activities in which he is interested. A reception in his honor was held at Glenn Dale Sanatorium on August 31 and among those who spoke were District Commissioner Renah F. Camalier and Health Officer Daniel L. Seckinger. Although relinquishing his past duties, Dr. Peabody accepted the position of consultant and will visit Glenn Dale once a week for conferences. Dr. Peabody had served as General Superintendent of Glenn Dale Sanatorium from 1934 to 1939 when he resigned to accept the part-time position of Chief Visiting Consultant.

Dr. Samuel Cohen, Jersey City, New Jersey, was recently appointed Director of Medicine at the B. S. Pollak Hospital for Chest Diseases in Jersey City.

Dr. Basil Papanicolaou, Athens, Greece, presented a series of lectures on tuberculosis in Istanbul, Turkey, at the invitation of the Turkish government and the World Health Organization.

Dr. Juan J. Castillo, Havana, Cuba, was appointed Director of the Hospital-Sanatorio La Esperanza, the largest anti-tuberculosis institution in Cuba, by President Fulgencio Batista.

Dr. Gerrit W. Schepers, Johannesburg, South Africa, has been appointed Director of the Saranac Laboratory of the Trudeau-Saranac Institute. Dr. Gordon M. Meade, formerly Medical Director of the Trudeau Sanatorium, was appointed Executive Director.

Dr. Arthur Q. Penta, Schenectady, New York, Director of the Department of Bronchoesophagology, St. Clare and Ellis Hospitals, was recently elected President of the Schenectady County Medical Society.

Dr. Ada Chree Reid, New York City, retiring editor of the *Journal of the American Medical Women's Association*, received a citation from the American Medical Women's Association in appreciation of her outstanding service to the journal and to the advancement of the interests of the association.

Dr. Leo G. Rigler, head of the Radiology Department, University of Minnesota, spoke at the University's convocation November 12 on the subject, "India: Masses, Mores and Medicine." Dr. Rigler visited India last February under the sponsorship of the World Health Organization and the Unitarian Service Committee.

Dr. Harold A. Lyons was appointed Director of the University Division of Chest Service at Kings County Hospital, Brooklyn, New York. Dr. Lyons is Associate Professor of Medicine at the State University College of Medicine at New York City.

Dr. Francis L. Lederer, Professor and Head of the Department of Otolaryngology, University of Illinois, College of Medicine, spoke at the 18th International Medical Assembly of Southwest Texas in San Antonio, January 26-28.

Dr. Bernard P. Wolff, Georgia, recently presented two lectures at the Forest Hills Division, Veterans Administration Hospital, Atlanta, on "Phthisiogenesis".

Dr. Louis L. Friedman, Birmingham, Alabama, spoke before the staff conference at the Batty State Hospital, Rome, Georgia, December 17 on "Pneumoconiosis in Soft Coal Workers".

Dr. Carl C. Aven, Atlanta, Georgia, spoke at the annual press conference of high school editors in Atlanta. He stressed the need for hospital beds for tuberculosis.

ANNOUNCEMENTS

Hoffman-LaRoche, Inc. announces Gantricillin 'Roche', a new cherry-flavored antibacterial especially useful for children. Each 5 cc. (teaspoonful) of Gantricillin (acetyl)-200 suspension contains 200,000 units of penicillin G potassium plus 0.5 Gm. of Gantrisin, the highly soluble, wide-spectrum, single sulfonamine, in the form of Gantrisin (acetyl).

Untiring efforts to develop an antibiotic with a wide antimicrobial range, and relatively free from side-effects, have resulted in the discovery of Achromycin by Lederle Laboratories. Achromycin is closely related to Aureomycin, differing in the replacement of the chlorine atom in the structure by the hydrogen atom. Indications are that the antibacterial range of Achromycin is as great as any antibiotic tried to date, and may well be useful in treating some of the rickettsial and viral infections. Preliminary studies by several investigators have indicated considerably fewer side reactions than have been observed with other broad-spectrum antibiotics.

The first preparation for metabolic control of obesity, protecting the already-damaged liver of the overweight person, has been made available to the medical profession by Lakeside Laboratories. Called Obelip, the product contains important lipotropics which aid and protect the liver by curbing fatty deposition and mobilizing depot fat for metabolic burning.

A "grown-up" tablet form of the vitamin B_{12}-B_1 product 'Trophite' was introduced recently by Smith, Kline & French Laboratories. The uses for which 'Trophite' has been prescribed since its introduction last year include shortening convalescence through increased appetite; treating the chronically ill or undernourished patient; and supplementing nutrition in chronic diarrhea and celiac disease.

MEDICAL SERVICE BUREAU

POSITIONS AVAILABLE

Senior staff physician wanted for 220 bed tuberculosis hospital using modern therapy including chest surgery. Annual stipend $6,552 to $7,800 with nominal deductions for apartment and maintenance. Based on qualifications, appointee may be started in second or third step. Apply Medical Superintendent, Pine Camp Hospital, Richmond, Virginia.

Tulare-Kings Counties Tuberculosis Hospital, Springville, California, offers approved residencies in pulmonary diseases. Excellent program in modern hospital, including non-tuberculous diseases. Salary $525.00 including furnished home for family. Apply to medical director.

Book Reviews

THE ESOPHAGUS AND ITS DISEASES. By Eddy D. Palmer, M.D., Chief Gastrointestinal Section, Walter Reed Army Hospital. Paul B. Hoeber, Inc., publisher, New York, 1952. P. 501, Price $15.00.

This comprehensive study of the esophagus is most timely. In the past the esophagus has been considered merely a connecting tube between the mouth and the rest of the gastrointestinal tract. Lt. Col. Palmer's very extensive experience with this vital organ is reflected in his excellent exposition of the esophagus and its diseases. A wide choice of x-ray material and diagramatic illustrations has been used to describe and emphasize important points. His style of writing is easy to read and his bibliography is most complete. In general the volume covers a tremendous quantity of material in a concise and yet thorough fashion.

Beginning most logically with the anatomy of the esophagus, the reader is immediately given a detailed gross and microscopic indoctrination into the peculiarities of this portion of the gastrointestinal tract. The anatomy of the lower portion of the esophagus, that segment which plays such an important part in functional diseases, is given special emphasis by the presentation of a rather detailed account of controversial opinion expressed by good workers in the field. This portion of the book is most advantageously illustrated. Progressing next to the clinical physiology, one travels through the complexities of deglutition and once again finds himself in the lower esophageal segment where the physiology of the controversial sphincter mechanism at the cardia is discussed in detail. With these two important considerations as a background, the author begins his discussion of esophageal disease with congenital defects, continues with discussions of anatomical abnormalities, both congenital and acquired, and then presents a complete, concise discussion of the important subjects of achalasia and cardiospasm. Special mention should be made of this chapter because the discussion of etiology and of treatment avoids a confusing, drawn-out discourse of conflicting opinion; the conclusions are presented and the reader is allowed to choose those which appeal to him. The chapter on carcinoma of the esophagus deals extensively with theories on etiology, the patho-physiology, and the treatment. Detail has been included in the discussion of pathology and symptomatology which would seem logical. The chapters on esophagitis due to corrosive agents and no strictures and webs are particularly good in the light of their very progressive approach to the important problem of lye strictures in children and the treatment thereof. The discussion of esophageal varices is valuable because of the discussion of various methods of treatment. Here the reader has a chance to evaluate opinions and statistics concerning all of the newer methods of treatment of esophageal varices, including resection of the involved segment and the much discussed porto-caval anastomoses. The chapters discussing peptic ulcer of the esophagus, and esophagitis related to other diseases is timely because the symptomatology resulting from these conditions frequently is mis-diagnosed or treated with little physiological reasoning behind the method of therapy. The author has attempted to correlate the pathophysiology with the resulting symptomatology and thereby approach therapy in as sound a way as possible. In several instances, however, the reader is left somewhat confused because definite answers have not been given, although this is the situation as it exists, through no fault of the author. The chapters discussing specific infections of the esophagus, such as tuberculosis, syphillis, the animal parasites, and the fungus diseases are somewhat scanty in detail because of the dearth of material that the author has observed and the little that has appeared in the literature on these subjects. In the case of the mycoses, a lack of understanding of the basic disease process was intimated.

This book represents a truly monumental piece of work and should well become a classic in the field of esophageal disease. The time and care which have gone

into the preparation of this book are evident in its wealth of valuable information. As a text for beginners in the field as well as a reference book for those better acquainted with gastrointestinal disease and as a guide to the roentgenologist and esophagoscopist, this book will be found unusually adequate. The general format, the printing and the illustrations are all excellent.

PAUL H. HOLINGER.

ASPECTS OF THE PSYCHOLOGY OF THE TUBERCULOUS. By Gordon F. Derner, Ph.D. Paul B. Hoeber, Inc. Medical Book Department of Harper & Bros., Publishers, 1953. Price $3.50.

This psychosomatic medicine monograph of 119 pages by Gordon F. Derner, Ph.D., reports a limited clinical study of some psychological factors in persons with tuberculosis—factors arising from tuberculosis, including the disease itself and its concomitants. The study reflects a practical approach to the investigation of psychological aspects of a chronic disease once considered only within the realm of physical illness.

As stated by the author: This study attempts to describe and measure the general attitudes, feelings, personality factors, and intellectual factors found among hospitalized tuberculosis patients. It is not an attempt to give a picture of the unconscious psychodynamics which prepare the patient for tuberculosis nor an attempt to give a conclusive psychosomatic portrait. Careful investigation of consciously discernible behavior has been the basic intent. The specific questions it attempts to answer are:

1) What are some of the specific feelings of the tuberculous patient concerning his disease and his life in the sanatorium?
2) To what extent do tuberculous patients in a sanatorium have fears and anxieties about their disease?
3) How frequent are the fears of the tuberculous patient, and what are their nature?
4) What are the typical reactions to tuberculosis as shown by patients in a sanatorium?
5) To what extent are there personality deviations in the tuberculous patient?
6) How similar for all tuberculous patients are the personality deviations which are present?
7) To what extent is spes phthisica reported by the tuberculous patient?
8) What are the implications for the guidance and education of the tuberculous in the results of the study?

Those questions, principally, were posed and answered on the basis of a group of patients selected for the study. No time period is noted during which the study was conducted.

The investigated sample population was composed of 32 young adult white hospitalized pulmonary tuberculous patients, 10 males and 22 females, in the Tuberculosis Division of Grasslands Hospital in New York. The criteria for selection were that the patient be within the age range of 18 to 40 years, able to read and write English, hospitalized between 2 months and 2 years, a first admission for tuberculosis treatment, and not on the hospital serious list.

The author's broad method of investigation included clinical interviews, standard and specially devised psychological tests, and general information obtained from the patients' hospital record. Whenever possible the test responses of the sample group were compared with those of normal populations used as an indirect control population. Verbatim interview extracts picture realistically attitudes and feelings of the test group toward tuberculosis, the diagnosis, the symptoms, the treatment, and the effect of the disease on the person's life. The author emphasizes in his implications of findings that the approach to the tuberculous

patient should be therapeutic. The reviewer, on the contrary, prefers to place the emphasis on mental hygiene in both orientation and rehabilitation of tuberculous individuals, reserving psychotherapy only for special cases when indicated.

Dr. Derner suggests there is some relationship between psychological attitudes and the onset of disease and even a more marked relationship between attitudes and relapse but the precise nature of the relationship was not approached by the study.

Despite the small sample population chosen for examination, and notwithstanding Dr. Derner's naive and dogmatic generalizations based thereon, the monograph is important to professional workers, students and others interested in tuberculosis and in the general field of psychosomatic medicine. The book should be most profitable to all who are mindful of the manifest and manifold current needs for further exploration and elaboration of the psychological factors involved in the tuberculous person, the total therapeutic management and rehabilitation.

P. J. SPARER.

PENNSYLVANIA PIONEERS AGAINST TUBERCULOSIS. By Esther Gaskins Price. National Tuberculosis Association, New York, 1952. Pp. 294. Price $5.00.

The committee on archieves of the National Tuberculosis Association with Dr. Robert G. Patterson, Columbus, Ohio, as Secretary has done marvelous work in assembling, analyzing and presenting historical data on tuberculosis. This volume written by Esther Gaskins Price and published by the National Tuberculosis Association is number six in the historical series of publications.

It was important that the history of tuberculosis in Pennsylvania be recorded with particular reference to pioneer workers since it was there that the first state tuberculosis association was organized. The frontispiece is composed of an excellent photograph of Dr. Lawrence Flick, which is most appropriate since he was largely responsible for the state organization and he pioneered in so many other tuberculosis activities, including the founding of a free hospital for poor consumptives with a program based on the care of the tuberculous in special wards of general hospitals. A fine sketch is presented of Dr. Flick's early life. At the age of 17 years he was sent home from college because of tuberculosis. It was his personal experience with the disease which caused him to turn from law and enter the Jefferson Medical College in 1877. He had a burning desire to throw his energy of a life time into the fight against tuberculosis. He read the best of the writings of the world pertaining to this disease and had an unusual ability to ferret out fundamental information. Thus he early became a firm believer in the contagiousness of tuberculosis and immediately accepted Koch's announcement of the discovery of the tubercle bacillus. Therefore, he was convinced the disease must be fought on a contagious disease basis and worked unceasingly to that end.

The public must be informed and he saw that this was done through public addresses, pamphlets, etc. Although he was strenuously opposed by those who lacked adequate information, disciples slowly but surely gathered around him in ever increasing numbers. Then sanatorium building began in Philadelphia and in the state of Pennsylvania. Prevention was Flick's watchword, therefore, persons with tuberculosis must be found and registered and isolated in institutions. There must be state and local boards of health, he said, to serve as the official agents in the eradication of this disease.

In 1902, Henry Phipps, the philanthropist, had learned of the tuberculosis control movement and made himself known to Dr. Flick and asked to be shown the White Haven Sanatorium. He was so impressed that he sent some of the patients clothing. Then came a check for $5,000 to be used by Dr. Flick for the sanatorium. He later took Dr. Flick on a trip to study tuberculosis programs and institutions in England, France and Germany. When Dr. Flick expressed a desire to open a small clinic

on Lombard Street, Philadelphia, Mr. Phipps said, "Buy the block, I will stand back of you." This was the beginning of the Henry Phipps Institute for the study, treatment and prevention of tuberculosis which Dr. Flick visualized as a center from which education might radiate throughout the world, organizing a dispensary from which treatment and help through social service might be extended to the poor and bringing the International Congress on Tuberculosis to the United States for the stimulative effect it would have on the crusade.

Another pioneer destined to make significant contributions in tuberculosis control was Leonard Pearson, a young veterinarian, who, at the age of 23 years, launched a battle against the sale of milk and meat of infected cows. He administered the first tuberculin tests to cattle in the United States on a farm just outside of Philadelphia only five weeks before Dr. Flick founded the Pennsylvania Tuberculosis Society. Pearson's pioneer work led to the greatest campaign against tuberculosis in animals in history. It has resulted in almost complete eradication of tuberculosis in the cattle herds of this country.

The works of numerous other pioneers are presented. This book of 294 pages contains a tremendous volume of information from the beginning of the anti-tuberculosis activities to 1908. It is hoped that later monographs by the author will bring the fight against tuberculosis in Pennsylvania to date.

This book is written in such a fascinating style and its content is so authentic that it will be read with profit not only by tuberculosis workers everywhere but also by the general public.

J. ARTHUR MYERS.

HOLBROOK OF THE SAN. By Marjorie Freeman Campbell. Ryerson Press, publisher, Toronto, Canada.

This is the story of a man, an institution, and a disease. The man may be considered as representative of all men and women who pioneered against the disease. The institution—except for its size—is typical of all pioneer institutions founded to combat the disease. Leagued together, the men and women and the institutions they contrived—initially tents, shacks, even abandoned street cars—have waged an epic battle. This book is the story of that battle, the war that reduced the Great White Plague of 50 years ago to the white plague of today.

At the turn of the twentieth century every community in Canada could point to families whose children were wiped out by consumption one by one as they flowered into adolescence, for it was youth in its late teens that most appealed to the white death. Undoubtedly the memory of one such victim—a very beautiful young girl dying of consumption—whom his elders took him to visit when he was a mere child influenced John Howard Holbrook in his eventual choice of medicine as a profession. This and the sudden death from diabetes of his loved mother when he was five years old, and the consequent change in his fortunes, led to his later avowed "eagerness to discover more concerning the tragedies of consumption and diabetes."

In maintaining a book such as this within the bounds required by modern publishing trends and modern reading habits, many details must be severely limited or even omitted. The names of sanatoria throughout Canada, of members of the medical profession, of individuals and organizations which appear in these pages, have been chosen in preference to others fully as worthy, because of some unusual development, outstanding contribution, or long and devoted service. No one could regret more deeply than the author that the legion who have served as unselfishly in this field could not all have been included in this volume.

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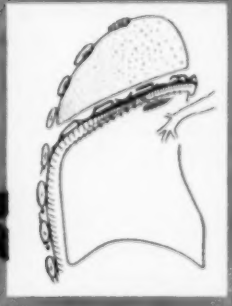
*Engberg, H., and Hansen, J. L.: Acta tuberc. Scandinav. 28:45, 1953.



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Internal Medicine — Diseases of the Chest — Pneumoconioses

1906 Ninth Avenue South Phone 54-3324 Birmingham, Alabama

COLLEGE EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

20th Annual Meeting, American College of Chest Physicians
Fairmont Hotel, San Francisco, California, June 17-20, 1954.

Third International Congress on Diseases of the Chest
American College of Chest Physicians
Council on International Affairs
Barcelona, Spain, October 4-8, 1954.

POSTGRADUATE COURSE

7th Annual Postgraduate Course on Diseases of the Chest
Bellevue-Stratford Hotel, Philadelphia, Pennsylvania, March 15-19, 1954.

CHAPTER MEETINGS

Louisiana Chapter (organizational meeting) New Orleans, February 15.
New Jersey Chapter, Jersey City, February 23.
Missouri Chapter, St. Louis, April 4.
Tennessee Chapter, Nashville, April 11.
Ohio Chapter, Columbus, April 13.
Alabama Chapter, Mobile, April 14.
Arizona Chapter, Chandler, April 24.
Florida Chapter, Hollywood, April 25.

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excellent toleration

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1. Sayer, R. J., et al.: Am. J. M. Sc. 221:206 (Mar.) 1951.
2. Welch, H.: Ann. New York Acad. Sc. 53:253 (Sept.) 1950.
3. Werner, C. A., et al.: Proc. Soc. Exper. Biol. & Med. 74:261 (June) 1950.
4. Wolman, B., et al.: Brit. M. J. 1:419 (Feb. 25) 1950.
5. Potterfield, T. G., et al.: J. Philadelphia Gen. Hosp. 2:6 (Jan.) 1951.
6. King, E. Q., et al.: J. A. M. A. 143:1 (May 6) 1950.

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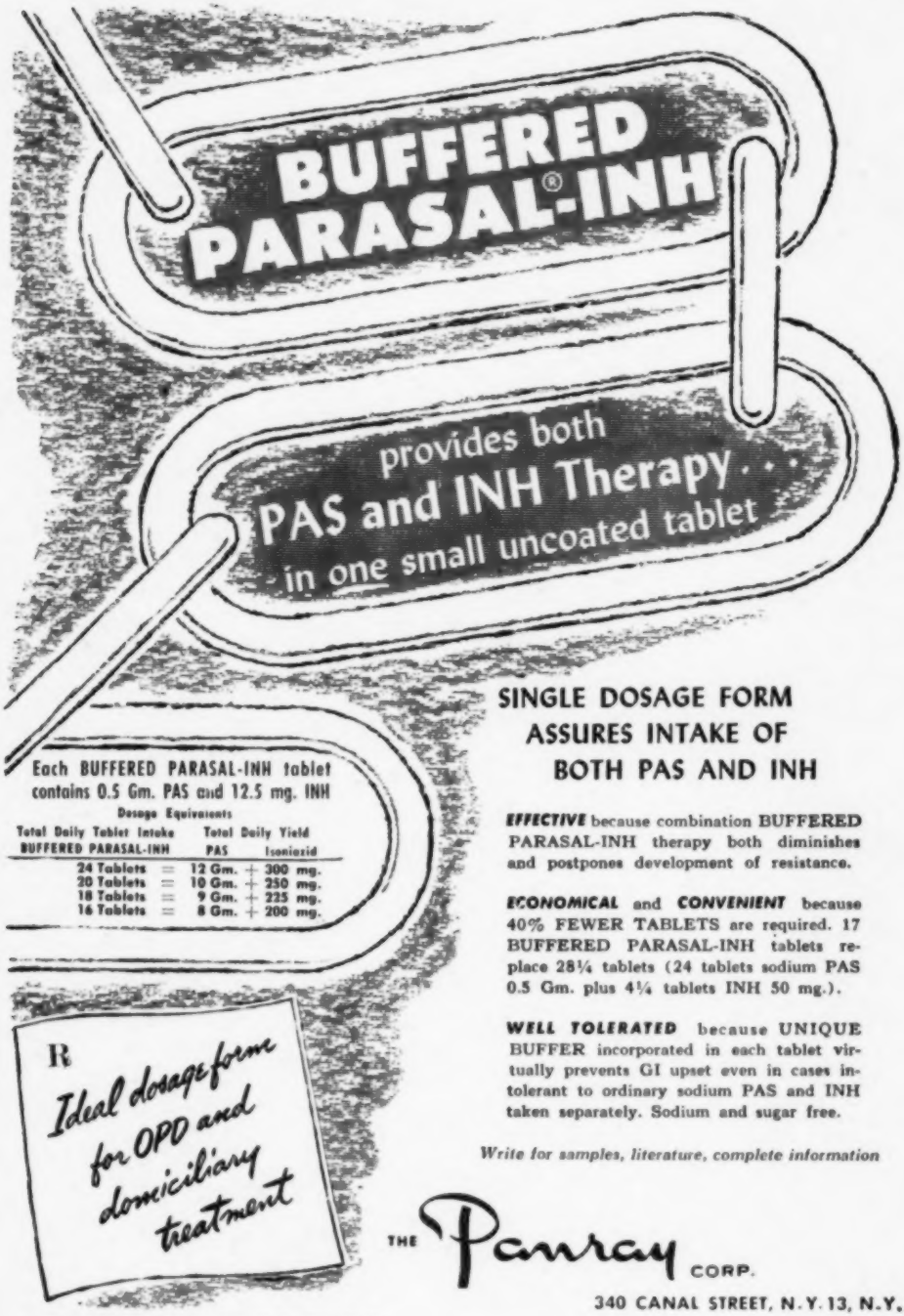

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